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FILE COVERS 1907 - 15 Aug 2002 VOL 137 ISS 7
FILE LAST UPDATED: 14 Aug 2002 (20020814/ED)

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```
=> d l56 all tot
```

L56 ANSWER 1 OF 15 HCAPLUS COPYRIGHT 2002 ACS
AN **2002:521933** HCAPLUS
TI **Antibodies** and **fragments** against epitopes present on **cancer**, **metastatic** or leukemia cells and platelets for diagnosis and therapy of **tumor**, **metastasis**, leukemia, autoimmune disease, and inflammation
IN Lazarovits, Janette; Hagai, Yocheved; Plaksin, Daniel; Vogel, Tikva; Nimrod, Abraham; Mar-Haim, Hagit; Szanthon, Ester; Richter, Tamar; Amit, Boaz; Kooperman, Lena; Peretz, Tuvia; Levanon, Avigdor
PA Bio-Technology General Corp., USA
SO PCT Int. Appl., 310 pp.
CODEN: PIXXD2
DT Patent
LA English
IC ICM C12N
CC 15-2 (Immunochemistry)
Section cross-reference(s): 1, 3, **8**, 9, 63

FAN.CNT 2

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2002053700	A2	20020711	WO 2001-US49442	20011231

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRAI US 2000-258948P P 20001229
US 2000-751181 A 20001229

AB The present invention provides epitopes present on **cancer** cells

and important in physiol. phenomena such as cell rolling, **metastasis**, and inflammation. Therapeutic and diagnostic methods and compns. using **antibodies** capable of **binding** to the epitopes are provided. The **antibodies** or **fragments** are capable of **binding** to, e.g. PSGL-1, fibrinogen .gamma. prime, GP1b.alpha., heparin, lumican, complement compd. 4 (CC4), interalpha inhibitor and prothrombin. Methods and compns. according to the present invention can be used in diagnosis of and therapy for such diseases as **cancer**, including **tumor** growth and **metastasis**, leukemia, auto-immune disease, and inflammatory disease.

ST **antibody fragment** epitope **cancer** **metastasis** platelet autoimmune disease inflammation

IT Leukemia
(B-cell, acute; **antibodies** and **fragments** against epitopes present on **cancer**, **metastatic** or leukemia cells and platelets for diagnosis and therapy of **tumor**, **metastasis**, leukemia, autoimmune disease, and inflammation)

IT Complement
RL: BSU (Biological study, unclassified); DGN (Diagnostic use); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(CC4; **antibodies** and **fragments** against epitopes present on **cancer**, **metastatic** or leukemia cells and platelets for diagnosis and therapy of **tumor**, **metastasis**, leukemia, autoimmune disease, and inflammation)

IT Antigens
RL: BSU (Biological study, unclassified); DGN (Diagnostic use); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(CD162; **antibodies** and **fragments** against epitopes present on **cancer**, **metastatic** or leukemia cells and platelets for diagnosis and therapy of **tumor**, **metastasis**, leukemia, autoimmune disease, and inflammation)

IT Antigens
RL: BSU (Biological study, unclassified); DGN (Diagnostic use); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(CD42; **antibodies** and **fragments** against epitopes present on **cancer**, **metastatic** or leukemia cells and platelets for diagnosis and therapy of **tumor**, **metastasis**, leukemia, autoimmune disease, and inflammation)

IT Immunoglobulins
RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified); DGN (Diagnostic use); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(G; **antibodies** and **fragments** against epitopes present on **cancer**, **metastatic** or leukemia cells and platelets for diagnosis and therapy of **tumor**, **metastasis**, leukemia, autoimmune disease, and inflammation)

IT Immunoglobulins
RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified); DGN (Diagnostic use); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(G; **antibodies** and **fragments** against epitopes present on **cancer**, **metastatic** or leukemia cells and platelets for diagnosis and therapy of **tumor**, **metastasis**, leukemia, autoimmune disease, and inflammation)

IT Glycolipoproteins
RL: BSU (Biological study, unclassified); DGN (Diagnostic use); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(GPIb.alpha.; **antibodies** and **fragments** against epitopes present on **cancer**, **metastatic** or leukemia cells and platelets for diagnosis and therapy of **tumor**, **metastasis**, leukemia, autoimmune disease, and inflammation)

IT Glycoproteins

RL: BSU (Biological study, unclassified); DGN (Diagnostic use); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(PSGL-1 (**P-selectin** glycoprotein ligand-1); **antibodies** and **fragments** against epitopes present on **cancer, metastatic** or leukemia cells and platelets for diagnosis and therapy of **tumor, metastasis,** leukemia, autoimmune disease, and inflammation)

IT Leukemia
(acute lymphocytic; **antibodies** and **fragments** against epitopes present on **cancer, metastatic** or leukemia cells and platelets for diagnosis and therapy of **tumor, metastasis,** leukemia, autoimmune disease, and inflammation)

IT Leukemia
(acute myelogenous; **antibodies** and **fragments** against epitopes present on **cancer, metastatic** or leukemia cells and platelets for diagnosis and therapy of **tumor, metastasis,** leukemia, autoimmune disease, and inflammation)

IT Platelet (blood)
(aggregation; **antibodies** and **fragments** against epitopes present on **cancer, metastatic** or leukemia cells and platelets for diagnosis and therapy of **tumor, metastasis,** leukemia, autoimmune disease, and inflammation)

IT Anti-infective agents
Antibacterial agents
Antitumor agents
Antiviral agents
Autoimmune disease
Cell aggregation
DNA sequences
Disulfide group
Drugs
Epitopes
Human
Imaging agents
Immunotherapy
Inflammation
Leukemia
Molecular cloning
Multiple myeloma
Peptidomimetics
Phage display library
Platelet (blood)
Protein sequences
Sulfation
Thrombolytics
Thrombosis
(**antibodies** and **fragments** against epitopes present on **cancer, metastatic** or leukemia cells and platelets for diagnosis and therapy of **tumor, metastasis,** leukemia, autoimmune disease, and inflammation)

IT **Antibodies**
RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified); DGN (Diagnostic use); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(**antibodies** and **fragments** against epitopes present on **cancer, metastatic** or leukemia cells and platelets for diagnosis and therapy of **tumor, metastasis,** leukemia, autoimmune disease, and inflammation)

IT Carbohydrates
Fibrinogens
Glycolipids
Glycoproteins
Lipids

Lipopolysaccharides
Lipoproteins
Peptides
Radionuclides
Toxins
RL: BSU (Biological study, unclassified); DGN (Diagnostic use); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(**antibodies** and **fragments** against epitopes present on **cancer**, **metastatic** or leukemia cells and platelets for diagnosis and therapy of **tumor**, **metastasis**, leukemia, autoimmune disease, and inflammation)

IT **Drug delivery systems**
(**carriers**; **antibodies** and **fragments** against epitopes present on **cancer**, **metastatic** or leukemia cells and platelets for diagnosis and therapy of **tumor**, **metastasis**, leukemia, autoimmune disease, and inflammation)

IT **Neoplasm**
(cell; **antibodies** and **fragments** against epitopes present on **cancer**, **metastatic** or leukemia cells and platelets for diagnosis and therapy of **tumor**, **metastasis**, leukemia, autoimmune disease, and inflammation)

IT **Artery, disease**
(coronary, restenosis; **antibodies** and **fragments** against epitopes present on **cancer**, **metastatic** or leukemia cells and platelets for diagnosis and therapy of **tumor**, **metastasis**, leukemia, autoimmune disease, and inflammation)

IT Test kits
(diagnostic; **antibodies** and **fragments** against epitopes present on **cancer**, **metastatic** or leukemia cells and platelets for diagnosis and therapy of **tumor**, **metastasis**, leukemia, autoimmune disease, and inflammation)

IT Cell **adhesion**
(disease assocd. with; **antibodies** and **fragments** against epitopes present on **cancer**, **metastatic** or leukemia cells and platelets for diagnosis and therapy of **tumor**, **metastasis**, leukemia, autoimmune disease, and inflammation)

IT Cardiovascular system
(disease; **antibodies** and **fragments** against epitopes present on **cancer**, **metastatic** or leukemia cells and platelets for diagnosis and therapy of **tumor**, **metastasis**, leukemia, autoimmune disease, and inflammation)

IT Immunity
(disorder; **antibodies** and **fragments** against epitopes present on **cancer**, **metastatic** or leukemia cells and platelets for diagnosis and therapy of **tumor**, **metastasis**, leukemia, autoimmune disease, and inflammation)

IT X-ray
(emitter; **antibodies** and **fragments** against epitopes present on **cancer**, **metastatic** or leukemia cells and platelets for diagnosis and therapy of **tumor**, **metastasis**, leukemia, autoimmune disease, and inflammation)

IT Pseudomonas
(exotoxin; **antibodies** and **fragments** against epitopes present on **cancer**, **metastatic** or leukemia cells and platelets for diagnosis and therapy of **tumor**, **metastasis**, leukemia, autoimmune disease, and inflammation)

IT Toxins
RL: BSU (Biological study, unclassified); DGN (Diagnostic use); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(exotoxins, Pseudomonas; **antibodies** and **fragments** against epitopes present on **cancer**, **metastatic** or leukemia cells and platelets for diagnosis and therapy of **tumor**, **metastasis**, leukemia, autoimmune disease, and inflammation)

IT Immunoglobulins
RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified); DGN (Diagnostic use); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(**fragments**; **antibodies** and **fragments** against epitopes present on **cancer**, **metastatic** or leukemia cells and platelets for diagnosis and therapy of **tumor**, **metastasis**, leukemia, autoimmune disease, and inflammation)

IT Glycoproteins
RL: BSU (Biological study, unclassified); DGN (Diagnostic use); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(glycocalicins; **antibodies** and **fragments** against epitopes present on **cancer**, **metastatic** or leukemia cells and platelets for diagnosis and therapy of **tumor**, **metastasis**, leukemia, autoimmune disease, and inflammation)

IT Immunoglobulins
RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified); DGN (Diagnostic use); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(heavy chains; **antibodies** and **fragments** against epitopes present on **cancer**, **metastatic** or leukemia cells and platelets for diagnosis and therapy of **tumor**, **metastasis**, leukemia, autoimmune disease, and inflammation)

IT Purpura (disease)
(idiopathic thrombocytopenic; **antibodies** and **fragments** against epitopes present on **cancer**, **metastatic** or leukemia cells and platelets for diagnosis and therapy of **tumor**, **metastasis**, leukemia, autoimmune disease, and inflammation)

IT **Drug delivery systems**
(**immunoconjugates**; **antibodies** and **fragments** against epitopes present on **cancer**, **metastatic** or leukemia cells and platelets for diagnosis and therapy of **tumor**, **metastasis**, leukemia, autoimmune disease, and inflammation)

IT Diagnosis
(immunodiagnosis; **antibodies** and **fragments** against epitopes present on **cancer**, **metastatic** or leukemia cells and platelets for diagnosis and therapy of **tumor**, **metastasis**, leukemia, autoimmune disease, and inflammation)

IT Heart, disease
(infarction; **antibodies** and **fragments** against epitopes present on **cancer**, **metastatic** or leukemia cells and platelets for diagnosis and therapy of **tumor**, **metastasis**, leukemia, autoimmune disease, and inflammation)

IT Immunoglobulins
RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified); DGN (Diagnostic use); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(light chains; **antibodies** and **fragments** against epitopes present on **cancer**, **metastatic** or leukemia cells and platelets for diagnosis and therapy of **tumor**, **metastasis**, leukemia, autoimmune disease, and inflammation)

IT Polymers
RL: BSU (Biological study, unclassified); DGN (Diagnostic use); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(lipophilic; **antibodies** and **fragments** against epitopes present on **cancer**, **metastatic** or leukemia cells and platelets for diagnosis and therapy of **tumor**, **metastasis**, leukemia, autoimmune disease, and inflammation)

IT **Drug delivery systems**
(**liposomes**; **antibodies** and **fragments** against epitopes present on **cancer**, **metastatic** or leukemia cells and platelets for diagnosis and therapy of **tumor**

, **metastasis**, leukemia, autoimmune disease, and inflammation)

IT Proteoglycans
RL: BSU (Biological study, unclassified); DGN (Diagnostic use); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(lumicans; **antibodies** and **fragments** against epitopes present on **cancer**, **metastatic** or leukemia cells and platelets for diagnosis and therapy of **tumor**, **metastasis**, leukemia, autoimmune disease, and inflammation)

IT **Neoplasm**
(**metastasis**, cell; **antibodies** and **fragments** against epitopes present on **cancer**, **metastatic** or leukemia cells and platelets for diagnosis and therapy of **tumor**, **metastasis**, leukemia, autoimmune disease, and inflammation)

IT Gene
RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified); DGN (Diagnostic use); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(open reading frame; **antibodies** and **fragments** against epitopes present on **cancer**, **metastatic** or leukemia cells and platelets for diagnosis and therapy of **tumor**, **metastasis**, leukemia, autoimmune disease, and inflammation)

IT Linking agents
(peptide; **antibodies** and **fragments** against epitopes present on **cancer**, **metastatic** or leukemia cells and platelets for diagnosis and therapy of **tumor**, **metastasis**, leukemia, autoimmune disease, and inflammation)

IT **Artery, disease**
(restenosis; **antibodies** and **fragments** against epitopes present on **cancer**, **metastatic** or leukemia cells and platelets for diagnosis and therapy of **tumor**, **metastasis**, leukemia, autoimmune disease, and inflammation)

IT Eye, disease
(retinopathy; **antibodies** and **fragments** against epitopes present on **cancer**, **metastatic** or leukemia cells and platelets for diagnosis and therapy of **tumor**, **metastasis**, leukemia, autoimmune disease, and inflammation)

IT Animal cell
(rolling; **antibodies** and **fragments** against epitopes present on **cancer**, **metastatic** or leukemia cells and platelets for diagnosis and therapy of **tumor**, **metastasis**, leukemia, autoimmune disease, and inflammation)

IT Interferons
RL: BSU (Biological study, unclassified); DGN (Diagnostic use); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(.alpha.; **antibodies** and **fragments** against epitopes present on **cancer**, **metastatic** or leukemia cells and platelets for diagnosis and therapy of **tumor**, **metastasis**, leukemia, autoimmune disease, and inflammation)

IT 442605-19-8
RL: PRP (Properties)
(Unclaimed; **antibodies** and **fragments** against epitopes present on **cancer**, **metastatic** or leukemia cells and platelets for diagnosis and therapy of **tumor**, **metastasis**, leukemia, autoimmune disease, and inflammation)

IT 442598-74-5P 442598-75-6P 442598-76-7P 442598-77-8P 442598-81-4P 442598-82-5P
RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified); DGN (Diagnostic use); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(amino acid sequence; **antibodies** and **fragments** against epitopes present on **cancer**, **metastatic** or leukemia cells and platelets for diagnosis and therapy of **tumor**, **metastasis**, leukemia, autoimmune disease, and inflammation)

IT 212783-31-8 268723-76-8 268723-77-9 442527-61-9 442528-29-2
442528-30-5 442528-31-6 442528-32-7 442528-33-8 442528-34-9
442528-35-0
RL: BSU (Biological study, unclassified); DGN (Diagnostic use); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(**antibodies** and **fragments** against epitopes present on **cancer, metastatic** or leukemia cells and platelets for diagnosis and therapy of **tumor, metastasis**, leukemia, autoimmune disease, and inflammation)

IT 9001-26-7, Prothrombin 9005-49-6, Heparin 39346-44-6, Inter-.alpha.-trypsin inhibitor 40704-75-4 75037-46-6, gelonin
RL: BSU (Biological study, unclassified); DGN (Diagnostic use); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(**antibodies** and **fragments** against epitopes present on **cancer, metastatic** or leukemia cells and platelets for diagnosis and therapy of **tumor, metastasis**, leukemia, autoimmune disease, and inflammation)

IT 50-18-0, Cyclophosphamide 50-35-1, Thalidomide 50-78-2, Aspirin 53-03-2, Prednisone 53-86-1, Indomethacin 57-22-7, Vincristine 58-85-5, Biotin 127-07-1, Hydroxyurea 147-94-4, Cytarabine 305-03-3, Chlorambucil 9004-54-0, Dextran 9004-61-9, Hyaluronic acid 9013-20-1, Streptavidin 9041-08-1, Dalteparin sodium 10043-66-0, iodine-131 10098-91-6, yttrium-90 11056-06-7, Bleomycin 13968-53-1, ruthenium-103 13981-56-1, fluorine-18 13982-78-0, mercury-203 14041-48-6, thulium-165 14119-09-6, gallium-67 14133-76-7, technetium-99 14158-32-8, iodine-126 14304-79-1, tellurium-121 14331-95-4, ruthenium-105 14390-71-7, tellurium-122 14390-73-9, tellurium-125 14391-22-1, thulium-167 14834-67-4, iodine-133 14885-78-0, indium-113 14900-13-1, thulium-168 14932-42-4, xenon-133 15307-86-5, Diclofenac 15663-27-1, cis-Platinum 15678-91-8, krypton-81 15687-27-1, Ibuprofen 15715-08-9, iodine-123 15750-15-9, indium-111 15756-62-4, ruthenium-95 15757-14-9, gallium-68 15758-35-7, ruthenium-97 15765-39-6, bromine-77 15776-20-2, bismuth-213 20830-81-3, Daunorubicin 21679-14-1, Fludarabine 22204-53-1, Naproxen 23214-92-8, Doxorubicin 25316-40-9, Adriamycin 30516-87-1, Zidovudine 33069-62-4, Taxol 33369-51-6 35014-81-4, rhenium-199 38194-50-2, Sulindac 51146-56-6, Dexibuprofen 51633-78-4, mercury-167 51692-52-5, rhenium-201 51692-56-9, rhenium-205 51803-78-2, Nimesulide 52549-17-4, Pranoprofen 58957-92-9, Idarubicin 59277-89-3, Acyclovir 68206-94-0, Cloricromene 73963-72-1, Cilostazol 74397-12-9, Limaprost 74711-43-6, Zaltoprofen 75706-12-6, Leflunomide 80790-68-7, Morpholinodoxorubicin 82410-32-0, Ganciclovir 83712-60-1, Defibrotide 85622-93-1, Temozolomide 90101-16-9, Droxicam 113440-58-7, Calicheamicin 117989-72-7, OM 89 162011-90-7, Rofecoxib 169590-42-5, Celecoxib 173146-27-5, Denileukin diftitox 425603-01-6, WinRho SDF
RL: DGN (Diagnostic use); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(**antibodies** and **fragments** against epitopes present on **cancer, metastatic** or leukemia cells and platelets for diagnosis and therapy of **tumor, metastasis**, leukemia, autoimmune disease, and inflammation)

IT 2543-43-3
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(linker polypeptide; **antibodies** and **fragments** against epitopes present on **cancer, metastatic** or leukemia cells and platelets for diagnosis and therapy of **tumor, metastasis**, leukemia, autoimmune disease, and inflammation)

IT 442598-78-9P 442598-80-3P
RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified); DGN (Diagnostic use); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(nucleotide sequence; **antibodies** and **fragments** against epitopes present on **cancer, metastatic** or

leukemia cells and platelets for diagnosis and therapy of **tumor**, **metastasis**, leukemia, autoimmune disease, and inflammation)

IT 442605-56-3
RL: PRP (Properties)
(unclaimed nucleotide sequence; **antibodies** and **fragments** against epitopes present on **cancer**, **metastatic** or leukemia cells and platelets for diagnosis and therapy of **tumor**, **metastasis**, leukemia, autoimmune disease, and inflammation)

IT 442604-60-6 442604-62-8 442604-63-9 442604-64-0 442604-65-1
442604-66-2 442604-67-3 442604-68-4 442604-69-5 442604-70-8
442604-71-9 442604-72-0 442604-73-1 442604-74-2 442604-75-3
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RL: PRP (Properties)
(unclaimed protein sequence; **antibodies** and **fragments** against epitopes present on **cancer**, **metastatic** or leukemia cells and platelets for diagnosis and therapy of **tumor**, **metastasis**, leukemia, autoimmune disease, and inflammation)

IT 122024-47-9 149298-29-3 245330-86-3 245330-96-5 245331-07-1
245331-15-1 245331-22-0 245331-32-2 245331-36-6 245331-39-9
245331-51-5 245331-68-4 245331-74-2 245332-10-9 245333-35-1
245333-43-1 245333-53-3 245333-62-4 245333-65-7 245333-66-8
245333-74-8 245333-75-9 245333-76-0 245333-82-8 245333-90-8
245333-98-6 245334-15-0 245334-24-1 245334-37-6 245334-46-7
245334-69-4 245334-81-0 245334-95-6 245335-03-9 245335-22-2
245335-28-8 245335-54-0 245448-41-3 245448-42-4 245448-43-5
245448-44-6 245448-45-7 245448-46-8 245448-47-9 245448-48-0
245448-49-1 245448-50-4 245448-51-5 245448-52-6 245448-53-7
245448-54-8 245448-55-9 245448-56-0 245448-57-1 245448-58-2
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245448-96-8 245448-97-9 245448-98-0 245448-99-1 245449-00-7
245449-01-8 245449-02-9 245449-03-0 245449-04-1 245449-05-2
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245449-11-0 245449-12-1 245449-13-2 245449-15-4 268723-83-7
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442527-60-8 442527-62-0 442527-63-1 442527-64-2 442527-65-3
442527-66-4 442527-67-5 442527-68-6 442527-69-7 442527-70-0
442527-71-1 442527-72-2 442527-73-3 442527-74-4 442527-75-5
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442605-44-9 442605-45-0 442605-46-1 442605-47-2 442605-48-3
442605-49-4 442605-50-7 442605-51-8 442605-52-9 442605-53-0
442605-54-1 442605-55-2 442605-57-4 442701-09-9
RL: PRP (Properties)
(unclaimed sequence; **antibodies** and **fragments** against epitopes present on **cancer**, **metastatic** or leukemia cells and platelets for diagnosis and therapy of **tumor**, **metastasis**, leukemia, autoimmune disease, and inflammation)

L56 ANSWER 2 OF 15 HCAPLUS COPYRIGHT 2002 ACS
AN 2002:350656 HCAPLUS

TI **Targeting drugs** to irradiated tissue
AU **Kiani, M. F.**; Chen, X.; Burch, E. E.; Yuan, H.; Yokley, A.; **Goetz, D. J.**
CS School of Biomedical Engineering and Department of Radiation Oncology, University of Tennessee Health Science Center, Memphis, TN, 38163, USA
SO Proceedings - 28th International Symposium on Controlled Release of Bioactive Materials and 4th Consumer & Diversified Products Conference, San Diego, CA, United States, June 23-27, 2001 (2001), Volume 2, 1366-1367
Publisher: Controlled Release Society, Minneapolis, Minn.
CODEN: 69CNY8
DT Conference
LA English
CC 63 (Pharmaceuticals)
AB Certain **endothelial cell adhesion mols.** are up-regulated in tissue that has been irradiated for therapeutic purposes. This up-regulation of **endothelial cell adhesion mols.** provides a potential avenue for **targeting drugs** to select tissues. We have shown that model **drug carriers** can be selectively **targeted** to irradiated **endothelial** cells in vitro and irradiated cerebral microvasculature in vivo. Our data suggest that radiation-induced up-regulation of **endothelial cell adhesion mols.** may be exploited to **target drugs** and/or genes to select segments of the **endothelium**
.

RE.CNT 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD
RE
(1) Handschel, J; Int J Radiat Oncol Biol Phys 1999, V45, P475 HCAPLUS
(2) Prabhakarpandian, B; Submitted 2000
(3) Springer, T; Cell 1994, V76, P301 HCAPLUS

L56 ANSWER 3 OF 15 HCAPLUS COPYRIGHT 2002 ACS
AN **2002:293488** HCAPLUS
DN **136:314976**
TI **Targeted** therapeutic and ~~imaging agents~~
IN Li, King Chuen; Bednarski, Mark David; Wartchow, Charles Aaron; Pease, John S.; Dechene, Neal Edward; Trulson, Julie; Shen, Zhi Min
PA Targesome, Inc., USA
SO PCT Int. Appl., 94 pp.
CODEN: PIXXD2
DT Patent
LA English
IC ICM A61K051-00
CC 63-5 (Pharmaceuticals)
Section cross-reference(s): **8**, 15
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2002030473	A1	20020418	WO 2001-US31824	20011011

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

US 2002071843	A1	20020613	US 2001-976254	20011011
PRAI US 2000-239684P	P	20001011		

AB Therapeutic and imaging agents which are comprised of a **targeting** entity, a therapeutic or treatment entity and a linking **carrier** are provided. The linking **carrier** imparts addnl. advantages to

the therapeutic agents, which are not provided by conventional linking methods. Preferred agents of the present invention comprise a lipid construct, vesicle, **liposome**, or polymd. **liposome**. In some cases, the therapeutic or treatment entity is a **radioisotope**, **chemotherapeutic** agent, prodrug, toxin, or gene encoding a protein that exhibits cell toxicity. Preferably, the agent is further comprised of a stabilizing entity that imparts addnl. advantages to the therapeutic or imaging agent.

ST **drug targeting liposome antitumor radioisotope** imaging

IT **Cell adhesion molecules**
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(**ICAM-1** (**intercellular adhesion mol. 1**), **antibodies** to; **targeted** therapeutic and imaging agents)

IT Encephalomyelitis
(autoimmune; **targeted** therapeutic and imaging agents)

IT **Drug delivery systems**
(**carriers**; **targeted** therapeutic and imaging agents)

IT Polymers, biological studies
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(coated; **targeted** therapeutic and imaging agents)

IT Gene, animal
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(**cytotoxin**-encoding; **targeted** therapeutic and imaging agents)

IT Toxins
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(**cytotoxins**; **targeted** therapeutic and imaging agents)

IT **Blood vessel**
(**endothelium**, receptors of; **targeted** therapeutic and imaging agents)

IT **Drug delivery systems**
(**liposomes, pharmaceutical**; **targeted** therapeutic and imaging agents)

IT Encapsulation
(microencapsulation; **targeted** therapeutic and imaging agents)

IT Angiogenesis
(neovascularization; **targeted** therapeutic and imaging agents)

IT **Neoplasm**
(neovasculature of; **targeted** therapeutic and imaging agents)

IT **Blood vessel**
(neovasculature; **targeted** therapeutic and imaging agents)

IT Receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(of vascular **endothelium**; **targeted** therapeutic and imaging agents)

IT **Drug delivery systems**
(prodrugs; **targeted** therapeutic and imaging agents)

IT Carbohydrates, biological studies
Dendritic polymers
Peptides, biological studies
RGD peptides
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(**targetable**; **targeted** therapeutic and imaging agents)

IT **Antitumor** agents
Body fluid
Chelating agents
Drug delivery systems
Drug targeting
Drugs

Gene therapy
Imaging agents
Immunoradiotherapy
Scintigraphy
Stabilizing agents
(**targeted** therapeutic and imaging agents)

IT **Antibodies**
Ligands
Nucleic acids
Polyoxyalkylenes, biological studies
Radionuclides
Toxins
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(**targeted** therapeutic and imaging agents)

IT Antigens
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(**tumor**-specific antigens; **targeted** therapeutic and imaging agents)

IT Integrins
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(.alpha.v.beta.3; **targeted** therapeutic and imaging agents)

IT 324740-00-3, LM 609
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(LM 609; **targeted** therapeutic and imaging agents)

IT 121826-06-0, MX-DTPA
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(MX-DTPA; **targeted** therapeutic and imaging agents)

IT 27456-64-0P, Poly(Glu-Lys)
RL: PNU (Preparation, unclassified); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(**targeted** therapeutic and imaging agents)

IT 67-43-6, Dtpa 67-43-6D, DTPA, isothiocyanato deriv. 77-92-9, Citric acid, biological studies 7440-65-5, Yttrium 89, biological studies 9004-54-0, Dextran, biological studies 10098-91-6, Yttrium 90, biological studies 14133-76-7, Technetium 99, biological studies 14158-31-7, Iodine 125, biological studies 14683-23-9, Europium 152, biological studies 15750-15-9, Indium 111, biological studies 25104-18-1, Polylysine 25322-68-3, Polyethylene glycol 38000-06-5, Polylysine 52352-27-9, Poly(hydroxybutyric acid) 60239-18-1, Dota
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(**targeted** therapeutic and imaging agents)

RE.CNT 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD
RE
(1) Klaveness; US 6261537 B1 2001 HCAPLUS

L56 ANSWER 4 OF 15 HCAPLUS COPYRIGHT 2002 ACS
AN **2002:293471** HCAPLUS
DN **136:330520**
TI **Targeting drug**/gene **carriers** to **irradiated** tissue
IN **Kiani, Mohammad F.; Goetz, Douglas J.**
PA The University of Tennessee Research Corporation, USA
SO PCT Int. Appl., 52 pp.
CODEN: PIXXD2
DT Patent
LA English
IC ICM A61K039-00
ICS A61K039-395
CC 63-5 (Pharmaceuticals)
Section cross-reference(s): 3, **8**, 15

FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE

PI WO 2002030456 A1 20020418 WO 2001-US31881 20011012
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG
US 2002044959 A1 20020418 US 2001-975899 20011012
PRAI US 2000-239666P P 20001012
AB The present invention provides a biomol. **carrier** of **pharmaceuticals**, comprising: a biomol. **carrier** bearing mols. that **bind** to a **cellular adhesion mol.** expressed on **endothelial** cells, and a **pharmaceutical**. The present invention also provides a method of treating a pathophysiol. state in an individual in need of such treatment, comprising the steps of: **irradiating** a **target** tissue or organ in said individual; and administering to said individual the biomol. **carrier** disclosed herein.
ST gene **targeting drug irradiated** tissue
IT **Selectins**
RL: BSU (Biological study, unclassified); PEP (Physical, engineering or chemical process); PYP (Physical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(**E-; targeting drug** or gene **carriers** to **irradiated** tissue)
IT Animal cell line
(HUVEC; **targeting drug** or gene **carriers** to **irradiated** tissue)
IT **Cell adhesion molecules**
RL: BSU (Biological study, unclassified); PEP (Physical, engineering or chemical process); PYP (Physical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(**ICAM-1** (**intercellular adhesion mol. 1**); **targeting drug** or gene **carriers** to **irradiated** tissue)
IT **Selectins**
RL: BSU (Biological study, unclassified); PEP (Physical, engineering or chemical process); PYP (Physical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(**P-; targeting drug** or gene **carriers** to **irradiated** tissue)
IT **Cell adhesion molecules**
RL: BSU (Biological study, unclassified); PEP (Physical, engineering or chemical process); PYP (Physical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(**PECAM-1; targeting drug** or gene **carriers** to **irradiated** tissue)
IT **Cell adhesion molecules**
RL: BSU (Biological study, unclassified); PEP (Physical, engineering or chemical process); PYP (Physical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(**VCAM-1; targeting drug** or gene **carriers** to **irradiated** tissue)
IT **Drug delivery systems**
(**carriers; targeting drug** or gene **carriers** to **irradiated** tissue)
IT **Artery, disease**
(coronary, restenosis; **targeting drug** or gene **carriers** to **irradiated** tissue)
IT Cardiovascular system

(disease, arteriovenous malformation; **targeting drug** or gene **carriers** to **irradiated** tissue)

IT **Blood vessel**
(**endothelium**; **targeting drug** or gene **carriers** to **irradiated** tissue)

IT Cytometry
(flow; **targeting drug** or gene **carriers** to **irradiated** tissue)

IT Immunoglobulins
RL: BSU (Biological study, unclassified); PEP (Physical, engineering or chemical process); PYP (Physical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(**fragments**; **targeting drug** or gene **carriers** to **irradiated** tissue)

IT **Drug delivery systems**
(**liposomes**; **targeting drug** or gene **carriers** to **irradiated** tissue)

IT Eye, disease
(macula, degeneration; **targeting drug** or gene **carriers** to **irradiated** tissue)

IT **Drug delivery systems**
(**microbubbles**; **targeting drug** or gene **carriers** to **irradiated** tissue)

IT **Drug delivery systems**
(microspheres; **targeting drug** or gene **carriers** to **irradiated** tissue)

IT **Drug delivery systems**
(nanospheres; **targeting drug** or gene **carriers** to **irradiated** tissue)

IT **Artery, disease**
(restenosis; **targeting drug** or gene **carriers** to **irradiated** tissue)

IT **Antitumor** agents
Brain
Drug targeting
Drugs
Gene **targeting**
Human
Neoplasm
Radiotherapy
(**targeting drug** or gene **carriers** to **irradiated** tissue)

IT **Antibodies**
RL: BSU (Biological study, unclassified); PEP (Physical, engineering or chemical process); PYP (Physical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(**targeting drug** or gene **carriers** to **irradiated** tissue)

IT **Cell adhesion molecules**
Gene
RL: PEP (Physical, engineering or chemical process); PYP (Physical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(**targeting drug** or gene **carriers** to **irradiated** tissue)

IT Polyesters, biological studies
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(**targeting drug** or gene **carriers** to **irradiated** tissue)

IT 9003-53-6, Polystyrene
RL: PEP (Physical, engineering or chemical process); PYP (Physical process); TEM (Technical or engineered material use); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)

(microparticles; **targeting drug** or gene **carriers** to **irradiated** tissue)
IT 24980-41-4D, Poly(.epsilon.-caprolactone), **antibody conjugates** 25248-42-4D, Poly[oxy(1-oxo-1,6-hexanediyl)], **antibody conjugates** 28158-18-1D, **antibody conjugates**
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(**targeting drug** or gene **carriers** to **irradiated** tissue)
RE.CNT 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD
RE
(1) Hallahan; US 5962424 A 1999 HCAPLUS

L56 ANSWER 5 OF 15 HCAPLUS COPYRIGHT 2002 ACS
AN 2001:400679 HCAPLUS
DN 135:247100
TI Limited **adhesion** of biodegradable microspheres to **E-** and **P-selectin** under flow
AU Dickerson, J. Bradley; Blackwell, Jonathan E.; Ou, Jao J.; Patil, Vivek R. Shinde; **Goetz, Douglas J.**
CS Department of Biomedical Engineering, University of Memphis, Memphis, TN, USA
SO Biotechnology and Bioengineering (2001), 73(6), 500-509
CODEN: BIBIAU; ISSN: 0006-3592
PB John Wiley & Sons, Inc.
DT Journal
LA English
CC 63-5 (Pharmaceuticals)
AB In a variety of disease settings the expression of the **endothelial selectins E-** and **P-selectin** appears to be increased. This feature makes these mols. attractive **targets** around which to design directed **drug-delivery** schemes. One possible approach for achieving such **delivery** is to use polymeric biodegradable microspheres bearing a humanized monoclonal **antibody** (MAb) for **E-** and **P-selectin**, MAb HuEP5C7.g2. Perhaps the simplest technique for "coupling" HuEP5C7.g2 to the microspheres is via nonspecific adsorption. Previous studies suggest, however, that the adsorption of proteins onto microspheres fabricated in the presence of a stabilizer such as poly(vinyl alc.) (PVA) is limited. It is unclear to what extent this limited level of adsorbed HuEP5C7.g2 would be able to support **adhesion** to **E-** and **P-selectin** under flow conditions. To explore this issue, we prepd. microspheres from the biodegradable polymer, poly(.epsilon.-caprolactone) (PCL), using a single emulsion process and PVA as a stabilizer. We then incubated the PCL microspheres with HuEP5C7.g2 and studied the **adhesion** of the resulting HuEP5C7.g2 microspheres to **E-** and **P-selectin** under in vitro flow conditions. We found that the HuEP5C7.g2 PCL microspheres exhibit specific **adhesion** to Chinese hamster ovary cells stably expressing **P-selectin** (CHO-**P**) and 4-h IL-1.beta.-activated human umbilical vein **endothelial** cells (HUVEC). In contrast, HuEP5C7.g2 PCL microspheres exhibit little **adhesion** to parental CHO cells or inactivated HUVEC. The attachment efficiency to the **selectin** substrates was quite low, with appreciable attachment occurring only at low shear (0.3 dyn/cm2). Other supporting data strongly suggest that the limited attachment efficiency is due to a low level of HuEP5C7.g2 adsorbed to the PCL microspheres. Although the attachment was limited, a significant percentage of the HuEP5C7.g2 PCL microspheres were able to remain adherent at relatively high shear (8 dyn/cm2). Combined, our data suggest that HuEP5C7.g2 PCL microspheres exhibit selective limited **adhesion** to cellular substrate expressing **E-** and **P-selectin**.

ST polycaprolactone microsphere **antibody selectin adhesion**

IT **Selectins**
RL: BPR (Biological process); BSU (Biological study, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(**E-**; limited **adhesion** of biodegradable microspheres to **E-** and **P-selectin** under flow)

IT Animal cell line
(HUVEC; limited **adhesion** of biodegradable microspheres to **E-** and **P-selectin** under flow)

IT **Selectins**
RL: BPR (Biological process); BSU (Biological study, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(**P-**; limited **adhesion** of biodegradable microspheres to **E-** and **P-selectin** under flow)

IT Polyesters, biological studies
RL: BPR (Biological process); BSU (Biological study, unclassified); POF (Polymer in formulation); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(caprolactone-based; limited **adhesion** of biodegradable microspheres to **E-** and **P-selectin** under flow)

IT **Vein**
(**endothelium**; limited **adhesion** of biodegradable microspheres to **E-** and **P-selectin** under flow)

IT **Adhesion**, biological
Drug targeting
(limited **adhesion** of biodegradable microspheres to **E** - and **P-selectin** under flow)

IT **Drug delivery systems**
(microspheres; limited **adhesion** of biodegradable microspheres to **E-** and **P-selectin** under flow)

IT **Antibodies**
RL: PEP (Physical, engineering or chemical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(monoclonal, fo **selectins**; limited **adhesion** of biodegradable microspheres to **E-** and **P-selectin** under flow)

IT 24980-41-4, Poly(.epsilon.-caprolactone) 25248-42-4, Poly[oxy(1-oxo-1,6-hexanediyl)]
RL: BPR (Biological process); BSU (Biological study, unclassified); POF (Polymer in formulation); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(limited **adhesion** of biodegradable microspheres to **E** - and **P-selectin** under flow)

IT 9002-89-5, PVA
RL: MOA (Modifier or additive use); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(limited **adhesion** of biodegradable microspheres to **E** - and **P-selectin** under flow)

RE.CNT 36 THERE ARE 36 CITED REFERENCES AVAILABLE FOR THIS RECORD

RE

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(3) Bendas, G; Pharm Acta Helv 1998, V73, P19
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L56 ANSWER 6 OF 15 HCAPLUS COPYRIGHT 2002 ACS
AN **2001:152506** HCAPLUS
DN **134:202693**
TI Peptides capable of modulating the function of CD66 (CEACAM) family members
IN Skubitz, Keith M.; Skubitz, Amy P. N.
PA USA
SO PCT Int. Appl., 102 pp.
CODEN: PIXXD2
DT Patent
LA English
IC ICM A61K038-04
ICS A61K038-17; A61K039-00; C07K007-00; C07K007-08; C07K014-435; C07K017-00
CC 1-7 (Pharmacology)
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2001013937	A1	20010301	WO 2000-US23482	20000825
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
	EP 1212075	A1	20020612	EP 2000-957846	20000825
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL				
PRAI	US 1999-150791P	P	19990826		
	US 1999-152501P	P	19990902		
	WO 2000-US23482	W	20000825		

AB Peptides are provided which are capable of modulating the function (e.g., signaling or adhesive activities) of CD66 (CEACAM) family members and/or their ligands.

ST peptide CD66 CEACAM modulation; signaling **adhesion** CD66 CEACAM peptide

IT CD antigens
Ligands
RL: BOC (Biological occurrence); BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); OCCU (Occurrence); PROC (Process)
(CD66; peptides modulating function of CD66 (CEACAM) family members)

IT Animal cell line
(HUVEC; peptides modulating function of CD66 (CEACAM) family members)

IT **Selectins**
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(L-; peptides modulating function of CD66 (CEACAM) family members)

IT Peptides, biological studies
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(analogs; peptides modulating function of CD66 (CEACAM) family members)

IT Cell
(and biomaterials, **carrier**; peptides modulating function of CD66 (CEACAM) family members)

IT Integrins
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(antigens CD11b; peptides modulating function of CD66 (CEACAM) family members)

IT Bacteria (Eubacteria)
Virus
(**binding** to cell; peptides modulating function of CD66 (CEACAM) family members)

IT Polymers, biological studies
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(**carrier**; peptides modulating function of CD66 (CEACAM) family members)

IT Epithelium
Immune system
(cell; peptides modulating function of CD66 (CEACAM) family members)

IT DNA
Enzymes, biological studies
Lipids, biological studies
Proteins, specific or class
RNA
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(**conjugates**, with peptides; peptides modulating function of CD66 (CEACAM) family members)

IT Peptides, biological studies
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(**conjugates**; peptides modulating function of CD66 (CEACAM) family members)

IT Inflammation
Neoplasm
(detection; peptides modulating function of CD66 (CEACAM) family members)

IT **Blood vessel**
(**endothelium**, cell; peptides modulating function of CD66

(CEACAM) family members)
IT Skin
(keratinocyte; peptides modulating function of CD66 (CEACAM) family members)
IT **Drug delivery systems**
(**liposomes**; peptides modulating function of CD66 (CEACAM) family members)
IT Lymphocyte
(lymphokine-activated killer cell; peptides modulating function of CD66 (CEACAM) family members)
IT **Antitumor** agents
(**metastasis**; peptides modulating function of CD66 (CEACAM) family members)
IT **Drug delivery systems**
(microbeads; peptides modulating function of CD66 (CEACAM) family members)
IT Lymphocyte
(natural killer cell; peptides modulating function of CD66 (CEACAM) family members)
IT Anti-inflammatory agents
Antibacterial agents
Antitumor agents
Fluorescent substances
Radioactive substances
(peptide **conjugates**; peptides modulating function of CD66 (CEACAM) family members)
IT Angiogenesis
Angiogenesis inhibitors
B cell (lymphocyte)
Cell activation
Cell **adhesion**
Cell differentiation
Cell **proliferation**
Dendritic cell
Drug delivery systems
Immunomodulators
Neutrophil
T cell (lymphocyte)
(peptides modulating function of CD66 (CEACAM) family members)
IT Peptides, biological studies
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(peptides modulating function of CD66 (CEACAM) family members)
IT **Carcinoembryonic** antigen
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(peptides modulating function of CD66 (CEACAM) family members)
IT 328080-10-0D, analogs and **conjugates**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(8peptides modulating function of CD66 (CEACAM) family members)
IT 236733-25-8 236733-25-8D, analogs 273934-97-7 273934-97-7D, analogs and **conjugates** 273934-98-8 273934-98-8D, analogs and **conjugates** 273934-99-9 273934-99-9D, analogs and **conjugates** 328079-26-1 328079-26-1D, analogs and **conjugates** 328079-27-2 328079-27-2D, analogs and **conjugates** 328079-28-3 328079-28-3D, analogs and **conjugates** 328079-29-4 328079-29-4D, analogs and **conjugates** 328079-30-7 328079-30-7D, analogs and **conjugates** 328079-31-8 328079-31-8D, analogs and **conjugates** 328079-32-9 328079-32-9D, analogs and **conjugates** 328079-33-0 328079-33-0D, analogs and

conjugates	328079-34-1	328079-34-1D, analogs and
conjugates	328079-35-2	328079-35-2D, analogs and
conjugates	328079-36-3	328079-36-3D, analogs and
conjugates	328079-37-4	328079-37-4D, analogs and
conjugates	328079-38-5	328079-38-5D, analogs and
conjugates	328079-39-6	328079-39-6D, analogs and
conjugates	328079-40-9	328079-40-9D, analogs and
conjugates	328079-41-0	328079-41-0D, analogs and
conjugates	328079-42-1	328079-42-1D, analogs and
conjugates	328079-43-2	328079-43-2D, analogs and
conjugates	328079-44-3	328079-44-3D, analogs and
conjugates	328079-45-4	328079-45-4D, analogs and
conjugates	328079-46-5	328079-46-5D, analogs and
conjugates	328079-47-6	328079-47-6D, analogs and
conjugates	328079-48-7	328079-48-7D, analogs and
conjugates	328079-49-8	328079-49-8D, analogs and
conjugates	328079-50-1	328079-50-1D, analogs and
conjugates	328079-51-2	328079-51-2D, analogs and
conjugates	328079-52-3	328079-52-3D, analogs and
conjugates	328079-53-4	328079-53-4D, analogs and
conjugates	328079-54-5	328079-54-5D, analogs and
conjugates	328079-55-6	328079-55-6D, analogs and
conjugates	328079-56-7	328079-56-7D, analogs and
conjugates	328079-57-8	328079-57-8D, analogs and
conjugates	328079-58-9	328079-58-9D, analogs and
conjugates	328079-59-0	328079-59-0D, analogs and
conjugates	328079-60-3	328079-60-3D, analogs and
conjugates	328079-61-4	328079-61-4D, analogs and
conjugates	328079-62-5	328079-62-5D, analogs and
conjugates	328079-63-6	328079-63-6D, analogs and
conjugates	328079-64-7	328079-64-7D, analogs and
conjugates	328079-65-8	328079-65-8D, analogs and
conjugates	328079-66-9	328079-66-9D, analogs and
conjugates	328079-67-0	328079-67-0D, analogs and
conjugates	328079-68-1	328079-68-1D, analogs and
conjugates	328079-69-2	328079-69-2D, analogs and
conjugates	328079-70-5	328079-70-5D, analogs and
conjugates	328079-71-6	328079-71-6D, analogs and
conjugates	328079-72-7	328079-72-7D, analogs and
conjugates	328079-73-8	328079-73-8D, analogs and
conjugates	328079-74-9	328079-74-9D, analogs and
conjugates	328079-75-0	328079-75-0D, analogs and
conjugates	328079-76-1	328079-76-1D, analogs and
conjugates	328079-77-2	328079-77-2D, analogs and
conjugates	328079-78-3	328079-78-3D, analogs and
conjugates	328079-79-4	328079-79-4D, analogs and
conjugates	328079-80-7	328079-80-7D, analogs and
conjugates	328079-81-8	328079-81-8D, analogs and
conjugates	328079-82-9	328079-82-9D, analogs and
conjugates	328079-83-0	328079-83-0D, analogs and
conjugates	328079-84-1	328079-84-1D, analogs and
conjugates	328079-85-2	328079-85-2D, analogs and
conjugates	328079-86-3	328079-86-3D, analogs and
conjugates	328079-87-4	328079-87-4D, analogs and
conjugates	328079-88-5	328079-88-5D, analogs and
conjugates	328079-89-6	328079-89-6D, analogs and
conjugates	328079-90-9	328079-90-9D, analogs and
conjugates	328079-91-0	328079-91-0D, analogs and
conjugates	328079-92-1	328079-92-1D, analogs and
conjugates	328079-93-2	328079-93-2D, analogs and
conjugates	328079-94-3	328079-94-3D, analogs and
conjugates	328079-95-4	328079-95-4D, analogs and
conjugates	328079-96-5	328079-96-5D, analogs and

conjugates 328079-97-6 328079-97-6D, analogs and
conjugates 328079-98-7 328079-98-7D, analogs and
conjugates 328079-99-8 328079-99-8D, analogs and
conjugates 328080-00-8 328080-00-8D, analogs and
conjugates 328080-01-9 328080-01-9D, analogs and
conjugates 328080-02-0 328080-02-0D, analogs and
conjugates 328080-03-1 328080-03-1D, analogs and
conjugates 328080-04-2 328080-04-2D, analogs and
conjugates 328080-05-3 328080-05-3D, analogs and
conjugates 328080-06-4 328080-06-4D, analogs and
conjugates 328080-07-5 328080-07-5D, analogs and
conjugates 328080-08-6 328080-08-6D, analogs and
conjugates 328080-09-7 328080-09-7D, analogs and
conjugates 328080-10-0 328080-11-1 328080-11-1D, analogs and
conjugates 328080-12-2 328080-12-2D, analogs and
conjugates 328080-13-3 328080-13-3D, analogs and
conjugates 328080-14-4 328080-14-4D, analogs and
conjugates 328080-15-5 328080-15-5D, analogs and
conjugates 328080-16-6 328080-16-6D, analogs and
conjugates 328080-17-7 328080-17-7D, analogs and
conjugates 328080-18-8 328080-18-8D, analogs and
conjugates 328080-19-9 328080-19-9D, analogs and
conjugates 328080-20-2 328080-20-2D, analogs and
conjugates 328080-21-3 328080-21-3D, analogs and
conjugates 328080-22-4 328080-22-4D, analogs 328080-23-5
328080-23-5D, analogs 328080-24-6 328080-24-6D, analogs 328080-25-7
328080-25-7D, analogs 328080-26-8 328080-26-8D, analogs 328080-27-9
328080-27-9D, analogs 328080-28-0 328080-28-0D, analogs 328080-29-1
328080-29-1D, analogs 328080-30-4 328080-30-4D, analogs 328080-31-5
328080-31-5D, analogs 328080-32-6 328080-32-6D, analogs 328080-33-7
328080-33-7D, analogs 328080-34-8 328080-34-8D, analogs 328080-35-9
328080-35-9D, analogs 328080-36-0 328080-36-0D, analogs 328080-37-1
328080-37-1D, analogs 328080-38-2 328080-39-3 328080-40-6
328080-40-6D, analogs and **conjugates**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(peptides modulating function of CD66 (CEACAM) family members)

IT 328080-41-7 328080-42-8 328080-43-9 328080-44-0 328080-45-1
328080-46-2 328080-47-3 328080-48-4 328080-49-5 328080-50-8
328080-51-9 328080-52-0 328080-53-1 328080-54-2 328080-55-3
328080-56-4 328080-57-5 328080-58-6 328080-59-7 328080-60-0
328080-61-1 328080-62-2 328080-63-3 328080-64-4 328080-64-4D, analogs and **conjugates** 328080-65-5 328080-66-6 328080-67-7
328080-68-8 328080-69-9 328080-70-2 328080-71-3 328080-72-4
328080-73-5 328080-74-6 328080-75-7 328080-75-7D, analogs and **conjugates** 328080-76-8 328080-77-9 328080-78-0
328080-78-0D, analogs and **conjugates** 328080-79-1 328080-80-4
328080-81-5 328080-82-6 328080-83-7 328080-84-8 328080-85-9
328080-86-0 328080-87-1 328080-88-2 328080-89-3 328080-90-6
328080-91-7 328080-92-8 328080-92-8D, analogs and **conjugates**
328080-93-9 328080-93-9D, analogs and **conjugates**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(peptides modulating function of CD66 (CEACAM) family members)

IT 328528-86-5 328528-87-6 328528-88-7 328528-89-8 328528-90-1
328528-91-2 328528-92-3 328528-93-4 328528-94-5 328528-95-6
328528-96-7 328528-97-8 328528-98-9 328528-99-0 328529-00-6
328529-01-7 328529-02-8 328529-03-9 328529-04-0 328529-05-1
328529-06-2 328529-07-3 328529-08-4 328529-09-5 328529-10-8
328529-11-9
RL: PRP (Properties)

(unclaimed sequence; peptides capable of modulating the function of CD66 (CEACAM) family members)

RE.CNT 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD

RE

(1) Barnett; US 5571710 A 1996 HCAPLUS
(2) Bodmer; US 5965710 A 1999 HCAPLUS
(3) Skubitz; Journal of Immunology 2000, V164(8), P4257 HCAPLUS
(4) Skubitz; Molecular Biology of the Cell, abstract 452 1999, V10(supplemental), P78A
(5) Teixeira; Blood 1994, V84(1), P211 HCAPLUS

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AN **2000:790365** HCAPLUS

DN **133:355219**

TI X-ray guided **drug delivery**

IN Hallahan, Dennis E.

PA Vanderbilt University, USA

SO PCT Int. Appl., 135 pp.
CODEN: PIXXD2

DT Patent

LA English

IC ICM A61K051-00
ICS A61K049-00; A01N063-00; C12Q001-68; C12N015-85; C12N015-63; C07H021-04

CC 63-5 (Pharmaceuticals)
Section cross-reference(s): 1, 2, **8**, 15

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2000066182	A1	20001109	WO 2000-US11485	20000428
	W: AU, CA, JP, US				
	RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
	US 6159443	A	20001212	US 1999-302456	19990429
	EP 1194173	A1	20020410	EP 2000-935839	20000428
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
PRAI	US 1999-302456	A2	19990429		
	WO 2000-US11485	W	20000428		

AB A method of **delivering** an active agent to a **target** tissue, particularly **neoplastic** tissue, vascular anomaly or **tumor** tissue, in a vertebrate subject. The method includes the steps of exposing the **target** tissue to ionizing **radiation**; and administering a **delivery** vehicle to the vertebrate subject before, after, during, or combinations thereof, exposing the **target** tissue to the ionizing **radiation**. The **delivery** vehicle includes the active agent and **delivers** the agent to the **target** tissue. Representative **delivery** vehicles include platelets; leukocytes; proteins or peptides which **bind** activated platelets; **antibodies** which **bind** activated platelets; microspheres coated with proteins or peptides which **bind** activated platelets; **liposomes conjugated** to proteins or peptides, platelets, or leukocytes which **bind** activated platelets, or **antibodies** which **bind** activated platelets; and combinations thereof.

ST X ray guidance **drug delivery**

IT Glycoproteins, specific or class
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PEP (Physical, engineering or chemical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(CVF (cobra venom factor); X-ray guided **drug delivery**
)

IT Enzymes, biological studies
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(DNA-repairing; X-ray guided **drug delivery**)

IT **Selectins**
RL: BOC (Biological occurrence); BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); OCCU (Occurrence); PROC (Process)
(**E-**; X-ray guided **drug delivery**)

IT **Cell adhesion molecules**
RL: BOC (Biological occurrence); BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); OCCU (Occurrence); PROC (Process)
(**ICAM-1** (**intercellular adhesion mol. 1**); X-ray guided **drug delivery**
)

IT **Sarcoma**
(Kaposi's; X-ray guided **drug delivery**)

IT Toxins
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(ML-I (mistletoe lectin I); X-ray guided **drug delivery**)

IT **Selectins**
RL: BOC (Biological occurrence); BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); OCCU (Occurrence); PROC (Process)
(**P-**; X-ray guided **drug delivery**)

IT **Blood vessel**
(**P-selectin** accumulation in **irradiated**; X-ray guided **drug delivery**)

IT Proteins, specific or class
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(PAP (pokeweed antiviral protein); X-ray guided **drug delivery**)

IT **Radionuclides**, biological studies
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(**Radionuclides**; X-ray guided **drug delivery**
)

IT Venoms
(Russell's viper; X-ray guided **drug delivery**)

IT Alkylating agents, biological
Angiogenesis inhibitors
Antitumor agents
Brain, **neoplasm**
Chemotherapy
Drug targeting
Genetic vectors
Imaging agents
Radiotherapy
Virus vectors
(X-ray guided **drug delivery**)

IT Abrins
Cytokines
Hormones, animal, biological studies
Ricins
Steroids, biological studies
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES

(Uses)
(X-ray guided **drug delivery**)

IT Cardiolipins
Ceramides
Cerebrosides
Diglycerides
Fatty acids, biological studies
Gangliosides
Glycolipids
Lysophosphatidylcholines
Lysophosphatidylethanolamines
Monoglycerides
Phosphatidic acids
Phosphatidylcholines, biological studies
Phosphatidylethanolamines, biological studies
Phosphatidylglycerols
Phosphatidylinositols
Phosphatidylserines
Polyoxyalkylenes, biological studies
Sphingomyelins
RL: BPR (Biological process); BSU (Biological study, unclassified); PEP (Physical, engineering or chemical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(X-ray guided **drug delivery**)

IT Enhancer (genetic element)
Promoter (genetic element)
RL: PEP (Physical, engineering or chemical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(X-ray guided **drug delivery**)

IT Platelet (blood)
(activated; X-ray guided **drug delivery**)

IT **Carcinoma**
(**adenocarcinoma**; X-ray guided **drug delivery**
)

IT **Blood vessel, neoplasm**
(angiofibroma; X-ray guided **drug delivery**)

IT Nutrients
(anti-; X-ray guided **drug delivery**)

IT **Melanoma**
(benign intracranial; X-ray guided **drug delivery**)

IT **Radiotherapy**
(boron-neutron capture, reagents for; X-ray guided **drug delivery**)

IT Bladder
Lung, **neoplasm**
Mammary gland
Ovary, **neoplasm**
Pancreas, **neoplasm**
Prostate gland
Thyroid gland, **neoplasm**
(**carcinoma**; X-ray guided **drug delivery**)

IT **Drug delivery systems**
(**carriers**; X-ray guided **drug delivery**)

IT Intestine, **neoplasm**
(colon, **carcinoma**; X-ray guided **drug delivery**)

IT Intestine, **neoplasm**
(colorectal, **carcinoma**; X-ray guided **drug delivery**)

IT Anthracyclines
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(derivs.; X-ray guided **drug delivery**)

IT Toxins
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(diphtheria; X-ray guided **drug delivery**)

IT Leukocyte
(**drug delivery** vehicle; X-ray guided **drug delivery**)

IT **Antibodies**
Peptides, biological studies
Proteins, specific or class
RL: BPR (Biological process); BSU (Biological study, unclassified); PEP (Physical, engineering or chemical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(**drug delivery** vehicle; X-ray guided **drug delivery**)

IT X-ray
(emitters; X-ray guided **drug delivery**)

IT **Blood vessel**
(**endothelium, targeting** of; X-ray guided **drug delivery**)

IT Pseudomonas
(exotoxin of; X-ray guided **drug delivery**)

IT Toxins
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(exotoxins, Pseudomonas; X-ray guided **drug delivery**)

IT Neuroglia
(glioma; X-ray guided **drug delivery**)

IT **Blood vessel, neoplasm**
(hemangioma; X-ray guided **drug delivery**)

IT Liver, **neoplasm**
(**hepatoma**; X-ray guided **drug delivery**)

IT Polymers, biological studies
RL: BPR (Biological process); BSU (Biological study, unclassified); PEP (Physical, engineering or chemical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(hydrophilic; X-ray guided **drug delivery**)

IT **Radiosensitizers**, biological
(imaging agent contg.; X-ray guided **drug delivery**)

IT Toxins
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(imaging agent contg.; X-ray guided **drug delivery**)

IT Fluorescent substances
Paramagnetic materials
(imaging agents; X-ray guided **drug delivery**)

IT **Radionuclides**, biological studies
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(imaging agents; X-ray guided **drug delivery**)

IT Immunoassay
(immunol. staining; X-ray guided **drug delivery**)

IT **Drug delivery systems**
(**liposomes**; X-ray guided **drug delivery**)

IT Eye, disease
(macula, degeneration; X-ray guided **drug delivery**)

IT **Blood vessel**
(malformation; X-ray guided **drug delivery**)

IT **Neoplasm**
(**metastasis**; X-ray guided **drug delivery**)

IT **Drug delivery systems**
(microspheres; X-ray guided **drug delivery**)
IT Fibrinogens
RL: PRP (Properties)
(peptides; X-ray guided **drug delivery**)
IT Protamines
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(purothionins; X-ray guided **drug delivery**)
IT Kidney, **neoplasm**
(renal cell **carcinoma**; X-ray guided **drug delivery**)
IT Eye, disease
(retrolental fibroplasia; X-ray guided **drug delivery**)
IT Proteins, specific or class
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(saporins; X-ray guided **drug delivery**)
IT **Neoplasm**
(solid, **metastases**; X-ray guided **drug delivery**)
IT Ionizing **radiation**
(subjection of tissue to; X-ray guided **drug delivery**)
IT **Drug delivery systems**
(**targeted**; X-ray guided **drug delivery**)
IT Vipera russelli
(venom; X-ray guided **drug delivery**)
IT Alkaloids, biological studies
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(vinca; X-ray guided **drug delivery**)
IT Integrins
RL: BOC (Biological occurrence); BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); OCCU (Occurrence); PROC (Process)
(.beta.3; X-ray guided **drug delivery**)
IT 7440-06-4, Platinum, biological studies
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(193; X-ray guided **drug delivery**)
IT 153312-60-8, DORIE
RL: BPR (Biological process); BSU (Biological study, unclassified); PEP (Physical, engineering or chemical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(SNAP 5114; X-ray guided **drug delivery**)
IT 50-18-0, Cyclophosphamide 51-21-8, 5-Fluorouracil 54-62-6, Aminopterin 55-86-7, Nitrogen mustard 59-05-2, Methotrexate 68-76-8, Trenimon 106-51-4D, 1,4-Benzoquinone, derivs. 147-94-4, Cytosine arabinoside 148-82-3, Melphalan 305-03-3, Chlorambucil 443-48-1, Metronidazole 477-30-5, Demecolcine 865-21-4, Vinblastine 1404-00-8, Mitomycin 7440-16-6, Rhodium 103, biological studies 9001-86-9, Phospholipase c 9002-04-4, Thrombin 9002-05-5, Activated blood coagulation factor x 9014-02-2, Neocarzinostatin 10098-91-6, Yttrium 90, biological studies 11056-06-7, Bleomycin 12634-34-3, Macromomycin 13551-87-6, Misonidazole 13981-51-6, Mercury 197, biological studies 14119-24-5, Osmium 191, biological studies 14265-75-9, Lutetium 177, biological studies 14374-81-3, Germanium 71, biological studies 14378-26-8,

Rhenium 188, biological studies 14391-11-8, Gold 199, biological studies 14391-19-6, Terbium 161, biological studies 14391-96-9, Scandium 47, biological studies 14596-37-3, Phosphorus 32, biological studies 14683-06-8, Tin 121, biological studies 14687-61-7, Arsenic 77, biological studies 14913-49-6, Bismuth 212, biological studies 14914-68-2, Antimony 119, biological studies 14914-76-2, Cesium 131, biological studies 14981-64-7, Palladium 109, biological studies 14981-79-4, Praseodymium 143, biological studies 14998-63-1, Rhenium 186, biological studies 15092-94-1, Lead 212, biological studies 15663-27-1, Cisplatin 15749-66-3, Phosphorus 33, biological studies 15755-39-2, Astatine 211, biological studies 15757-86-5, Copper 67, biological studies 15760-04-0, Silver 111, biological studies 18378-89-7, Mithramycin 20830-81-3, Daunomycin 23109-05-9, .alpha.-Amanitin 23214-92-8, Doxorubicin 33419-42-0, Etoposide 36877-68-6, Nitroimidazole 37316-87-3, Activated blood coagulation factor ix 53643-48-4, Vindesine 65988-88-7, Modeccin 75037-46-6, Gelonin 91933-11-8, Volkensin
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(X-ray guided **drug delivery**)

IT 57-88-5, Cholesterol, biological studies 2462-63-7, Dope 9003-09-2, Polyvinylmethylether 9003-39-8, Polyvinylpyrrolidone 9004-62-0, Hydroxyethylcellulose 14357-21-2 25014-12-4, Polymethacrylamide 25322-68-3 25805-17-8, Polyethyloxazoline 26375-28-0 37353-59-6, Hydroxymethylcellulose 104162-48-3, Dotma 113669-21-9 137056-72-5, Dc-chol 153312-64-2, Dmrie 158606-68-9, Polyaspartamide 306284-11-7 306284-12-8
RL: BPR (Biological process); BSU (Biological study, unclassified); PEP (Physical, engineering or chemical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(X-ray guided **drug delivery**)

IT 89105-94-2P 119336-88-8P 305794-91-6P 305794-93-8P 305794-95-0P 305794-97-2P 305794-98-3P 305794-99-4P 305795-00-0P 305795-01-1P
RL: PEP (Physical, engineering or chemical process); PNU (Preparation, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); PROC (Process); USES (Uses)
(X-ray guided **drug delivery**)

IT 15678-91-8, Krypton 81, biological studies 15750-15-9, Indium 111, biological studies
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(X-ray guided **drug delivery**)

IT 9001-99-4, Ribonuclease
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(bovine pancreatic; X-ray guided **drug delivery**)

IT 12585-85-2, Positron
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(emitters; X-ray guided **drug delivery**)

IT 10043-66-0, Iodine 131, biological studies 14683-16-0, Iodine 132, biological studies 14687-25-3, Lead 203, biological studies 15776-19-9, Bismuth 206, biological studies
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(imaging agent contg.; X-ray guided **drug delivery**)

IT 13981-50-5, Cobalt 57, biological studies 13982-64-4, Strontium 87, biological studies 14093-04-0, Iron 52, biological studies 14119-09-6, Gallium 67, biological studies 14133-76-7, Technetium 99, biological studies 14885-78-0, Indium 113, biological studies 14903-02-7, Potassium 43, biological studies 15047-05-9, Cesium 129, biological studies 15715-08-9, Iodine 123, biological studies 15720-35-1, Cesium 127, biological studies 15757-14-9, Gallium 68, biological studies

15765-39-6, Bromine 77, biological studies 18268-34-3, Rubidium 81, biological studies
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(imaging agent contg.; X-ray guided **drug delivery**)
IT 9026-43-1, Protein kinase 80449-02-1, Tyrosine kinase
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(inhibitors; X-ray guided **drug delivery**)
IT 306277-82-7 306277-84-9 306277-85-0 306277-86-1
RL: PRP (Properties)
(unclaimed sequence; x-ray guided **drug delivery**)
RE.CNT 13 THERE ARE 13 CITED REFERENCES AVAILABLE FOR THIS RECORD
RE
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(2) Bender; Hybridoma 1995, V14(2), P129 MEDLINE
(3) Gurewich; US 5759542 A 1998 HCAPLUS
(4) Hallahan; Biochemical and Biophysical Research Communications 1995, V217(3), P784 HCAPLUS
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(10) Schieven; US 5693627 A 1997 HCAPLUS
(11) Song; Radiology 1974, V111, P213 HCAPLUS
(12) Stratton; J Nucl Med 1994, V35, P1731 MEDLINE
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L56 ANSWER 8 OF 15 HCAPLUS COPYRIGHT 2002 ACS
AN **2000:756484** HCAPLUS
DN **133:329593**
TI Low adenosine anti-sense oligonucleotide, compositions, kit and method for treatment of airway disorders associated with bronchoconstriction, lung inflammation, allergy(ies) and surfactant depletion
IN Nyce, Jonathan W.
PA East Carolina University, USA
SO PCT Int. Appl., 1592 pp.
CODEN: PIXXD2
DT Patent
LA English
IC ICM A61K
CC 1-9 (Pharmacology)
Section cross-reference(s): 3, 63
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2000062736	A2	20001026	WO 2000-US8020	20000324
	WO 2000062736	A3	20011011		
	W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
	BR 2000006019	A	20010313	BR 2000-6019	20000324
	EP 1168919	A2	20020109	EP 2000-919668	20000324
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
PRAI	US 1999-127958P	P	19990406		
	WO 2000-US8020	W	20000324		

OS MARPAT 133:329593

AB An in vivo method of selectively **delivering** a nucleic acid to a **target** gene or mRNA, comprises the topical administration, e.g. to the respiratory system, of a subject of a therapeutic amt. of an oligonucleotide (oligo) that is antisense to the initiation codon region, the coding region, the 5' or 3' intron-exon junctions or regions within 2 to 10 nucleotides of the junctions of the gene or antisense to a mRNA complementary to the gene in an amt. effective to reach the **target** polynucleotide and reducing or inhibiting expression. In addn. a method of treating an adenosine-mediated effect comprises topically administering to a subject an antisense oligo in an amt. effective to treat the respiratory, pulmonary, or airway disease. In order to minimize triggering adenosine receptors by their metab., the administered oligos have a low content of or are essentially free of adenosine. A **pharmaceutical** compn. and formulations comprise the oligo antisense to an adenosine receptor, genes and mRNAs encoding them, genomic and mRNA flanking regions, intron and exon borders and all regulatory and functionally related segments of the genes and mRNAs encoding the polypeptides, their salts and mixts. Various formulations contain a requisite **carrier**, and optionally other additives and biol. active agents. The low-adenosine or adenosine-free (des-A) agent for practicing the method of the invention may be prepd. by selecting a **target** gene(s), genomic flanking region(s), RNA(s) and/or polypeptide(s) assocd. with a disease(s) or condition(s) afflicting lung airways, obtaining the sequence of the mRNA(s) corresponding to the **target** gene(s) and/or genomic flanking region(s), and/or RNAs encoding the **target** polypeptide(s), selecting at least one segment of the mRNA which may be up to 60 % free of thymidine (T) and synthesizing one or more anti-sense oligonucleotide(s) to the mRNA segments which are free of adenosine (A) by substituting a universal base for A when present in the oligonucleotide. The agent may be prepd. by selection of **target** nucleic acid sequences with GC running stretches, which have low T content, and by optionally replacing A in the antisense oligonucleotides with a "Universal or alternative base". The agent, compn. and formulations are used for prophylactic, preventive and therapeutic treatment of ailments assocd. with impaired respiration, lung allergy(ies) and/or inflammation and depletion lung surfactant or surfactant hypoprodn., such as pulmonary vasoconstriction, inflammation, allergies, allergic rhinitis, asthma, impeded respiration, lung pain, cystic fibrosis, bronchoconstriction. The present treatment is suitable for administration in combination with other treatments, e.g. before, during and after other treatments, including **radiation**, **chemotherapy**, **antibody** therapy and surgery, among others. Alternatively, the present agent is effectively administered prophylactically or therapeutically by itself for conditions without known therapies or as a substitute for therapies exhibiting undesirable side effects. The treatment of this invention may be administered directly into the respiratory system of a subject so that the agent has direct access to the lungs, or by other effective routes of administration, e.g. topically, transdermally, by implantation, etc., in an amt. effective to reduce or inhibit the symptoms of the ailment.

ST respiratory disease antisense oligonucleotide sequence antiinflammatory

IT Oligonucleotides
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(2'-O-Me; low-adenosine antisense oligonucleotides for treatment of airway disorders assocd. with bronchoconstriction, lung inflammation, allergies, and surfactant depletion)

IT Oligonucleotides
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(5'-N-carbamate; low-adenosine antisense oligonucleotides for treatment of airway disorders assocd. with bronchoconstriction, lung inflammation, allergies, and surfactant depletion)

IT Transcription factors
RL: BOC (Biological occurrence); BSU (Biological study, unclassified); BIOL (Biological study); OCCU (Occurrence)
(AP-1 (activator protein 1), **targeted**; low-adenosine antisense oligonucleotides for treatment of airway disorders assocd. with bronchoconstriction, lung inflammation, allergies, and surfactant depletion)

IT Adenosine receptors
RL: BOC (Biological occurrence); BSU (Biological study, unclassified); BIOL (Biological study); OCCU (Occurrence)
(A1, **targeted**; low-adenosine antisense oligonucleotides for treatment of airway disorders assocd. with bronchoconstriction, lung inflammation, allergies, and surfactant depletion)

IT Adenosine receptors
RL: BOC (Biological occurrence); BSU (Biological study, unclassified); BIOL (Biological study); OCCU (Occurrence)
(A2A, **targeted**; low-adenosine antisense oligonucleotides for treatment of airway disorders assocd. with bronchoconstriction, lung inflammation, allergies, and surfactant depletion)

IT Adenosine receptors
RL: BOC (Biological occurrence); BSU (Biological study, unclassified); BIOL (Biological study); OCCU (Occurrence)
(A2B, **targeted**; low-adenosine antisense oligonucleotides for treatment of airway disorders assocd. with bronchoconstriction, lung inflammation, allergies, and surfactant depletion)

IT Adenosine receptors
RL: BOC (Biological occurrence); BSU (Biological study, unclassified); BIOL (Biological study); OCCU (Occurrence)
(A3, **targeted**; low-adenosine antisense oligonucleotides for treatment of airway disorders assocd. with bronchoconstriction, lung inflammation, allergies, and surfactant depletion)

IT Bradykinin receptors
RL: BOC (Biological occurrence); BSU (Biological study, unclassified); BIOL (Biological study); OCCU (Occurrence)
(B1, **targeted**; low-adenosine antisense oligonucleotides for treatment of airway disorders assocd. with bronchoconstriction, lung inflammation, allergies, and surfactant depletion)

IT Bradykinin receptors
RL: BOC (Biological occurrence); BSU (Biological study, unclassified); BIOL (Biological study); OCCU (Occurrence)
(B2, **targeted**; low-adenosine antisense oligonucleotides for treatment of airway disorders assocd. with bronchoconstriction, lung inflammation, allergies, and surfactant depletion)

IT Chemokine receptors
RL: BOC (Biological occurrence); BSU (Biological study, unclassified); BIOL (Biological study); OCCU (Occurrence)
(C-C (cysteine-cysteine chemokine receptors), **targeted**; low-adenosine antisense oligonucleotides for treatment of airway disorders assocd. with bronchoconstriction, lung inflammation, allergies, and surfactant depletion)

IT Chemokines
RL: MSC (Miscellaneous)
(C-C, receptors, CCR3, **targeted**; low-adenosine antisense oligonucleotides for treatment of airway disorders assocd. with bronchoconstriction, lung inflammation, allergies, and surfactant depletion)

IT Chemokines
RL: MSC (Miscellaneous)
(C-C, .beta., receptor CCR1, **targeted**; low-adenosine antisense oligonucleotides for treatment of airway disorders assocd.

with bronchoconstriction, lung inflammation, allergies, and surfactant depletion)

IT Chemokines
RL: BOC (Biological occurrence); BSU (Biological study, unclassified); BIOL (Biological study); OCCU (Occurrence)
(C-C, .beta., receptor CCR2, **targeted**; low-adenosine antisense oligonucleotides for treatment of airway disorders assocd. with bronchoconstriction, lung inflammation, allergies, and surfactant depletion)

IT Chemokines
RL: MSC (Miscellaneous)
(C-C, .beta., receptor CCR2, **targeted**; low-adenosine antisense oligonucleotides for treatment of airway disorders assocd. with bronchoconstriction, lung inflammation, allergies, and surfactant depletion)

IT **Selectins**
RL: BOC (Biological occurrence); BSU (Biological study, unclassified); BIOL (Biological study); OCCU (Occurrence)
(**E-, targeted**; low-adenosine antisense oligonucleotides for treatment of airway disorders assocd. with bronchoconstriction, lung inflammation, allergies, and surfactant depletion)

IT **Endothelin** receptors
RL: BOC (Biological occurrence); BSU (Biological study, unclassified); BIOL (Biological study); OCCU (Occurrence)
(ETA, **targeted**; low-adenosine antisense oligonucleotides for treatment of airway disorders assocd. with bronchoconstriction, lung inflammation, allergies, and surfactant depletion)

IT **Endothelin** receptors
RL: BOC (Biological occurrence); BSU (Biological study, unclassified); BIOL (Biological study); OCCU (Occurrence)
(ETB; low-adenosine antisense oligonucleotides for treatment of airway disorders assocd. with bronchoconstriction, lung inflammation, allergies, and surfactant depletion)

IT Proteins, specific or class
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(FK5-**binding, targeted**; low-adenosine antisense oligonucleotides for treatment of airway disorders assocd. with bronchoconstriction, lung inflammation, allergies, and surfactant depletion)

IT Transcription factors
RL: BOC (Biological occurrence); BSU (Biological study, unclassified); BIOL (Biological study); OCCU (Occurrence)
(GATA-3, **targeted**; low-adenosine antisense oligonucleotides for treatment of airway disorders assocd. with bronchoconstriction, lung inflammation, allergies, and surfactant depletion)

IT **Cell adhesion molecules**
RL: BOC (Biological occurrence); BSU (Biological study, unclassified); BIOL (Biological study); OCCU (Occurrence)
(**ICAM-1 (intercellular adhesion mol. 1), targeted**; low-adenosine antisense oligonucleotides for treatment of airway disorders assocd. with bronchoconstriction, lung inflammation, allergies, and surfactant depletion)

IT **Cell adhesion molecules**
RL: BOC (Biological occurrence); BSU (Biological study, unclassified); BIOL (Biological study); OCCU (Occurrence)
(**ICAM-2 (intercellular adhesion mol. 2), targeted**; low-adenosine antisense oligonucleotides for treatment of airway disorders assocd. with bronchoconstriction, lung inflammation, allergies, and surfactant depletion)

IT **Cell adhesion molecules**

RL: BOC (Biological occurrence); BSU (Biological study, unclassified);
BIOL (Biological study); OCCU (Occurrence)
(**ICAM**-3, **targeted**; low-adenosine antisense oligonucleotides for treatment of airway disorders assocd. with bronchoconstriction, lung inflammation, allergies, and surfactant depletion)

IT Immunoglobulin receptors
RL: BOC (Biological occurrence); BSU (Biological study, unclassified);
BIOL (Biological study); OCCU (Occurrence)
(IgE, high-affinity, **targeted**; low-adenosine antisense oligonucleotides for treatment of airway disorders assocd. with bronchoconstriction, lung inflammation, allergies, and surfactant depletion)

IT **Selectins**
RL: BOC (Biological occurrence); BSU (Biological study, unclassified);
BIOL (Biological study); OCCU (Occurrence)
(L-, **targeted**; low-adenosine antisense oligonucleotides for treatment of airway disorders assocd. with bronchoconstriction, lung inflammation, allergies, and surfactant depletion)

IT Integrins
RL: BOC (Biological occurrence); BSU (Biological study, unclassified);
BIOL (Biological study); OCCU (Occurrence)
(LPAM-1 (lymphocyte Peyer's patch high **endothelial** venule **adhesion** mol. 1), **targeted**; low-adenosine antisense oligonucleotides for treatment of airway disorders assocd. with bronchoconstriction, lung inflammation, allergies, and surfactant depletion)

IT Cytokines
RL: BOC (Biological occurrence); BSU (Biological study, unclassified);
BIOL (Biological study); OCCU (Occurrence)
(MBP (major basic protein), **targeted**; low-adenosine antisense oligonucleotides for treatment of airway disorders assocd. with bronchoconstriction, lung inflammation, allergies, and surfactant depletion)

IT Transcription factors
RL: BOC (Biological occurrence); BSU (Biological study, unclassified);
BIOL (Biological study); OCCU (Occurrence)
(NF-IL6 (nuclear factor interleukin 6), **targeted**; low-adenosine antisense oligonucleotides for treatment of airway disorders assocd. with bronchoconstriction, lung inflammation, allergies, and surfactant depletion)

IT Transcription factors
RL: BOC (Biological occurrence); BSU (Biological study, unclassified);
BIOL (Biological study); OCCU (Occurrence)
(NFAT-1 (nuclear factor, activated T-cell, 1), **targeted**; low-adenosine antisense oligonucleotides for treatment of airway disorders assocd. with bronchoconstriction, lung inflammation, allergies, and surfactant depletion)

IT Tachykinin receptors
RL: BOC (Biological occurrence); BSU (Biological study, unclassified);
BIOL (Biological study); OCCU (Occurrence)
(NK1, **targeted**; low-adenosine antisense oligonucleotides for treatment of airway disorders assocd. with bronchoconstriction, lung inflammation, allergies, and surfactant depletion)

IT Transcription factors
RL: BOC (Biological occurrence); BSU (Biological study, unclassified);
BIOL (Biological study); OCCU (Occurrence)
(Nf6B, **targeted**; low-adenosine antisense oligonucleotides for treatment of airway disorders assocd. with bronchoconstriction, lung inflammation, allergies, and surfactant depletion)

IT **Selectins**
RL: BOC (Biological occurrence); BSU (Biological study, unclassified);
BIOL (Biological study); OCCU (Occurrence)

(**P-, targeted**; low-adenosine antisense oligonucleotides for treatment of airway disorders assocd. with bronchoconstriction, lung inflammation, allergies, and surfactant depletion)

IT **Cell adhesion molecules**
RL: BOC (Biological occurrence); BSU (Biological study, unclassified); BIOL (Biological study); OCCU (Occurrence)
(**PECAM-1, targeted**; low-adenosine antisense oligonucleotides for treatment of airway disorders assocd. with bronchoconstriction, lung inflammation, allergies, and surfactant depletion)

IT Proteins, specific or class
RL: BOC (Biological occurrence); BSU (Biological study, unclassified); BIOL (Biological study); OCCU (Occurrence)
(STAT 4, **targeted**; low-adenosine antisense oligonucleotides for treatment of airway disorders assocd. with bronchoconstriction, lung inflammation, allergies, and surfactant depletion)

IT Proteins, specific or class
RL: BOC (Biological occurrence); BSU (Biological study, unclassified); BIOL (Biological study); OCCU (Occurrence)
(STAT 6, **targeted**; low-adenosine antisense oligonucleotides for treatment of airway disorders assocd. with bronchoconstriction, lung inflammation, allergies, and surfactant depletion)

IT **Cell adhesion molecules**
RL: BOC (Biological occurrence); BSU (Biological study, unclassified); BIOL (Biological study); OCCU (Occurrence)
(**VCAM-1, vascular cellular adhesion mol., targeted**; low-adenosine antisense oligonucleotides for treatment of airway disorders assocd. with bronchoconstriction, lung inflammation, allergies, and surfactant depletion)

IT **Drug delivery systems**
(aerosols; low-adenosine antisense oligonucleotides for treatment of airway disorders assocd. with bronchoconstriction, lung inflammation, allergies, and surfactant depletion)

IT Nose
(allergic rhinitis; low-adenosine antisense oligonucleotides for treatment of airway disorders assocd. with bronchoconstriction, lung inflammation, allergies, and surfactant depletion)

IT Integrins
RL: BOC (Biological occurrence); BSU (Biological study, unclassified); BIOL (Biological study); OCCU (Occurrence)
(antigens CD11a, **targeted**; low-adenosine antisense oligonucleotides for treatment of airway disorders assocd. with bronchoconstriction, lung inflammation, allergies, and surfactant depletion)

IT Integrins
RL: BOC (Biological occurrence); BSU (Biological study, unclassified); BIOL (Biological study); OCCU (Occurrence)
(antigens CD11b, **targeted**; low-adenosine antisense oligonucleotides for treatment of airway disorders assocd. with bronchoconstriction, lung inflammation, allergies, and surfactant depletion)

IT **Antibodies**
Immunoglobulins
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(antisense oligos for genes encoding; low-adenosine antisense oligonucleotides for treatment of airway disorders assocd. with bronchoconstriction, lung inflammation, allergies, and surfactant depletion)

IT Sialoglycoproteins
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)

(asialoglycoproteins, uptake agent; low-adenosine antisense oligonucleotides for treatment of airway disorders assocd. with bronchoconstriction, lung inflammation, allergies, and surfactant depletion)

IT Oligonucleotides
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(boranophosphate-linked; low-adenosine antisense oligonucleotides for treatment of airway disorders assocd. with bronchoconstriction, lung inflammation, allergies, and surfactant depletion)

IT Bronchi
(bronchitis; low-adenosine antisense oligonucleotides for treatment of airway disorders assocd. with bronchoconstriction, lung inflammation, allergies, and surfactant depletion)

IT Bronchi
(bronchoconstriction; low-adenosine antisense oligonucleotides for treatment of airway disorders assocd. with bronchoconstriction, lung inflammation, allergies, and surfactant depletion)

IT **Drug delivery systems**
(capsules; low-adenosine antisense oligonucleotides for treatment of airway disorders assocd. with bronchoconstriction, lung inflammation, allergies, and surfactant depletion)

IT Oligonucleotides
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(carbamates; low-adenosine antisense oligonucleotides for treatment of airway disorders assocd. with bronchoconstriction, lung inflammation, allergies, and surfactant depletion)

IT Oligonucleotides
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(carbonates; low-adenosine antisense oligonucleotides for treatment of airway disorders assocd. with bronchoconstriction, lung inflammation, allergies, and surfactant depletion)

IT **Drug delivery systems**
(**carriers**; low-adenosine antisense oligonucleotides for treatment of airway disorders assocd. with bronchoconstriction, lung inflammation, allergies, and surfactant depletion)

IT Nervous system
(central, receptors of; low-adenosine antisense oligonucleotides for treatment of airway disorders assocd. with bronchoconstriction, lung inflammation, allergies, and surfactant depletion)

IT RNA
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(chimeras; low-adenosine antisense oligonucleotides for treatment of airway disorders assocd. with bronchoconstriction, lung inflammation, allergies, and surfactant depletion)

IT Lung, disease
(chronic obstructive; low-adenosine antisense oligonucleotides for treatment of airway disorders assocd. with bronchoconstriction, lung inflammation, allergies, and surfactant depletion)

IT Proteins, specific or class
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(cyclosporin A-**binding**, **targeted**; low-adenosine antisense oligonucleotides for treatment of airway disorders assocd. with bronchoconstriction, lung inflammation, allergies, and surfactant depletion)

IT Leukotriene receptors
RL: BOC (Biological occurrence); BSU (Biological study, unclassified); BIOL (Biological study); OCCU (Occurrence)

(cysteine-contg., **targeted**; low-adenosine antisense oligonucleotides for treatment of airway disorders assocd. with bronchoconstriction, lung inflammation, allergies, and surfactant depletion)

IT Respiratory tract
(disease; low-adenosine antisense oligonucleotides for treatment of airway disorders assocd. with bronchoconstriction, lung inflammation, allergies, and surfactant depletion)

IT **Drug delivery systems**
(dragees; low-adenosine antisense oligonucleotides for treatment of airway disorders assocd. with bronchoconstriction, lung inflammation, allergies, and surfactant depletion)

IT **Drug delivery systems**
(emulsions; low-adenosine antisense oligonucleotides for treatment of airway disorders assocd. with bronchoconstriction, lung inflammation, allergies, and surfactant depletion)

IT **Drug delivery systems**
(enteric-coated; low-adenosine antisense oligonucleotides for treatment of airway disorders assocd. with bronchoconstriction, lung inflammation, allergies, and surfactant depletion)

IT Lymphokine receptors
RL: BOC (Biological occurrence); BSU (Biological study, unclassified); BIOL (Biological study); OCCU (Occurrence)
(eotaxin, **targeted**; low-adenosine antisense oligonucleotides for treatment of airway disorders assocd. with bronchoconstriction, lung inflammation, allergies, and surfactant depletion)

IT Genetic element
RL: BOC (Biological occurrence); BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); OCCU (Occurrence); PROC (Process)
(exon, -intron junction, **targeting** of; low-adenosine antisense oligonucleotides for treatment of airway disorders assocd. with bronchoconstriction, lung inflammation, allergies, and surfactant depletion)

IT Receptors
RL: BOC (Biological occurrence); BSU (Biological study, unclassified); BIOL (Biological study); OCCU (Occurrence)
(for **antibodies, targeted**; low-adenosine antisense oligonucleotides for treatment of airway disorders assocd. with bronchoconstriction, lung inflammation, allergies, and surfactant depletion)

IT Oligonucleotides
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(formacetals; low-adenosine antisense oligonucleotides for treatment of airway disorders assocd. with bronchoconstriction, lung inflammation, allergies, and surfactant depletion)

IT Secretion (process)
(hypo-, of lung surfactant; low-adenosine antisense oligonucleotides for treatment of airway disorders assocd. with bronchoconstriction, lung inflammation, allergies, and surfactant depletion)

IT **Drug delivery systems**
(implants; low-adenosine antisense oligonucleotides for treatment of airway disorders assocd. with bronchoconstriction, lung inflammation, allergies, and surfactant depletion)

IT Lung, disease
(infection; low-adenosine antisense oligonucleotides for treatment of airway disorders assocd. with bronchoconstriction, lung inflammation, allergies, and surfactant depletion)

IT Lung, disease
(inflammation; low-adenosine antisense oligonucleotides for treatment of airway disorders assocd. with bronchoconstriction, lung

inflammation, allergies, and surfactant depletion)

IT **Drug delivery systems**
(inhalants; low-adenosine antisense oligonucleotides for treatment of airway disorders assocd. with bronchoconstriction, lung inflammation, allergies, and surfactant depletion)

IT Medical goods
(inhalers; low-adenosine antisense oligonucleotides for treatment of airway disorders assocd. with bronchoconstriction, lung inflammation, allergies, and surfactant depletion)

IT Lung, **neoplasm**
Lung, **neoplasm**
(inhibitors; low-adenosine antisense oligonucleotides for treatment of airway disorders assocd. with bronchoconstriction, lung inflammation, allergies, and surfactant depletion)

IT Codons
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(initiation, **targeting** of; low-adenosine antisense oligonucleotides for treatment of airway disorders assocd. with bronchoconstriction, lung inflammation, allergies, and surfactant depletion)

IT **Drug delivery systems**
(injections, i.m.; low-adenosine antisense oligonucleotides for treatment of airway disorders assocd. with bronchoconstriction, lung inflammation, allergies, and surfactant depletion)

IT **Drug delivery systems**
(injections, s.c.; low-adenosine antisense oligonucleotides for treatment of airway disorders assocd. with bronchoconstriction, lung inflammation, allergies, and surfactant depletion)

IT Interleukin receptors
Interleukin receptors
RL: BOC (Biological occurrence); BSU (Biological study, unclassified); BIOL (Biological study); OCCU (Occurrence)
(interleukin 11, **targeted**; low-adenosine antisense oligonucleotides for treatment of airway disorders assocd. with bronchoconstriction, lung inflammation, allergies, and surfactant depletion)

IT Interleukin 1 receptors
Interleukin 1 receptors
RL: BOC (Biological occurrence); BSU (Biological study, unclassified); BIOL (Biological study); OCCU (Occurrence)
(interleukin 1.beta., **targeted**; low-adenosine antisense oligonucleotides for treatment of airway disorders assocd. with bronchoconstriction, lung inflammation, allergies, and surfactant depletion)

IT Interleukin receptors
Interleukin receptors
RL: BOC (Biological occurrence); BSU (Biological study, unclassified); BIOL (Biological study); OCCU (Occurrence)
(interleukin 9, **targeted**; low-adenosine antisense oligonucleotides for treatment of airway disorders assocd. with bronchoconstriction, lung inflammation, allergies, and surfactant depletion)

IT **Drug delivery systems**
(intraarticular; low-adenosine antisense oligonucleotides for treatment of airway disorders assocd. with bronchoconstriction, lung inflammation, allergies, and surfactant depletion)

IT **Drug delivery systems**
(intrabuccal; low-adenosine antisense oligonucleotides for treatment of airway disorders assocd. with bronchoconstriction, lung inflammation, allergies, and surfactant depletion)

IT **Drug delivery systems**
(intrathecal; low-adenosine antisense oligonucleotides for treatment of airway disorders assocd. with bronchoconstriction, lung inflammation,

allergies, and surfactant depletion)

IT **Drug delivery systems**
(**intratumoral**; low-adenosine antisense oligonucleotides for treatment of airway disorders assocd. with bronchoconstriction, lung inflammation, allergies, and surfactant depletion)

IT **Drug delivery systems**
(intrauterine; low-adenosine antisense oligonucleotides for treatment of airway disorders assocd. with bronchoconstriction, lung inflammation, allergies, and surfactant depletion)

IT Genetic element
RL: BOC (Biological occurrence); BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); OCCU (Occurrence); PROC (Process)
(intron, -exon junction, **targeting** of; low-adenosine antisense oligonucleotides for treatment of airway disorders assocd. with bronchoconstriction, lung inflammation, allergies, and surfactant depletion)

IT Proteins, specific or class
RL: BOC (Biological occurrence); BSU (Biological study, unclassified); BIOL (Biological study); OCCU (Occurrence)
(ligand-**binding**, **targeted**; low-adenosine antisense oligonucleotides for treatment of airway disorders assocd. with bronchoconstriction, lung inflammation, allergies, and surfactant depletion)

IT **Drug delivery systems**
(**liposomes**; low-adenosine antisense oligonucleotides for treatment of airway disorders assocd. with bronchoconstriction, lung inflammation, allergies, and surfactant depletion)

IT Allergy
Allergy inhibitors
Analgesics
Anti-inflammatory agents
Antioxidants
Antitumor agents
Bronchodilators
Buffers
Cystic fibrosis
DNA sequences
Dispersing agents
Drug targeting
Dyes
Emphysema
Fillers
Flavoring materials
Genetic vectors
Iontophoresis
Microcrystallites
Pain
Particle size distribution
Preservatives
Propellants (sprays and foams)
Pulmonary surfactant
Respiratory distress syndrome
Solvents
Surfactants
(low-adenosine antisense oligonucleotides for treatment of airway disorders assocd. with bronchoconstriction, lung inflammation, allergies, and surfactant depletion)

IT Antisense oligonucleotides
Oligonucleotides
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PEP (Physical, engineering or chemical process); PNU (Preparation, unclassified); PRP (Properties); THU (Therapeutic use); BIOL

(Biological study); PREP (Preparation); PROC (Process); USES (Uses)
(low-adenosine antisense oligonucleotides for treatment of airway disorders assocd. with bronchoconstriction, lung inflammation, allergies, and surfactant depletion)

IT Phosphorothioate oligonucleotides
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(low-adenosine antisense oligonucleotides for treatment of airway disorders assocd. with bronchoconstriction, lung inflammation, allergies, and surfactant depletion)

IT Ribozymes
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(low-adenosine antisense oligonucleotides for treatment of airway disorders assocd. with bronchoconstriction, lung inflammation, allergies, and surfactant depletion)

IT Essential oils
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(low-adenosine antisense oligonucleotides for treatment of airway disorders assocd. with bronchoconstriction, lung inflammation, allergies, and surfactant depletion)

IT Transplant and Transplantation
Transplant and Transplantation
(lung, rejection; low-adenosine antisense oligonucleotides for treatment of airway disorders assocd. with bronchoconstriction, lung inflammation, allergies, and surfactant depletion)

IT **Antitumor** agents
Antitumor agents
(lung; low-adenosine antisense oligonucleotides for treatment of airway disorders assocd. with bronchoconstriction, lung inflammation, allergies, and surfactant depletion)

IT Proteins, specific or class
RL: BOC (Biological occurrence); BSU (Biological study, unclassified); BIOL (Biological study); OCCU (Occurrence)
(**malignancy**-assocd., **targeted**; low-adenosine antisense oligonucleotides for treatment of airway disorders assocd. with bronchoconstriction, lung inflammation, allergies, and surfactant depletion)

IT Gene, animal
RL: BOC (Biological occurrence); BSU (Biological study, unclassified); BIOL (Biological study); OCCU (Occurrence)
(mas, **targeted**; low-adenosine antisense oligonucleotides for treatment of airway disorders assocd. with bronchoconstriction, lung inflammation, allergies, and surfactant depletion)

IT Oligonucleotides
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(methoxyethyl; low-adenosine antisense oligonucleotides for treatment of airway disorders assocd. with bronchoconstriction, lung inflammation, allergies, and surfactant depletion)

IT Oligonucleotides
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(methoxymethyl; low-adenosine antisense oligonucleotides for treatment of airway disorders assocd. with bronchoconstriction, lung inflammation, allergies, and surfactant depletion)

IT Oligonucleotides
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PRP (Properties); THU (Therapeutic use); BIOL

(Biological study); USES (Uses)
(methylimino; low-adenosine antisense oligonucleotides for treatment of airway disorders assocd. with bronchoconstriction, lung inflammation, allergies, and surfactant depletion)

IT Oligonucleotides
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(methylphosphonate-linked; low-adenosine antisense oligonucleotides for treatment of airway disorders assocd. with bronchoconstriction, lung inflammation, allergies, and surfactant depletion)

IT Chemokines
RL: BOC (Biological occurrence); BSU (Biological study, unclassified); BIOL (Biological study); OCCU (Occurrence)
(monocyte chemoattractant protein 3, **targeted**; low-adenosine antisense oligonucleotides for treatment of airway disorders assocd. with bronchoconstriction, lung inflammation, allergies, and surfactant depletion)

IT Chemokines
RL: BOC (Biological occurrence); BSU (Biological study, unclassified); BIOL (Biological study); OCCU (Occurrence)
(monocyte chemoattractant protein 4, **targeted**; low-adenosine antisense oligonucleotides for treatment of airway disorders assocd. with bronchoconstriction, lung inflammation, allergies, and surfactant depletion)

IT Chemokines
RL: BOC (Biological occurrence); BSU (Biological study, unclassified); BIOL (Biological study); OCCU (Occurrence)
(monocyte chemoattractant protein-2, **targeted**; low-adenosine antisense oligonucleotides for treatment of airway disorders assocd. with bronchoconstriction, lung inflammation, allergies, and surfactant depletion)

IT **Drug delivery systems**
(nasal; low-adenosine antisense oligonucleotides for treatment of airway disorders assocd. with bronchoconstriction, lung inflammation, allergies, and surfactant depletion)

IT Receptors
RL: BOC (Biological occurrence); BSU (Biological study, unclassified); BIOL (Biological study); OCCU (Occurrence)
(neutrophil adherence, **targeted**; low-adenosine antisense oligonucleotides for treatment of airway disorders assocd. with bronchoconstriction, lung inflammation, allergies, and surfactant depletion)

IT Cytokines
RL: BOC (Biological occurrence); BSU (Biological study, unclassified); BIOL (Biological study); OCCU (Occurrence)
(neutrophil chemotactic factor, **targeted**; low-adenosine antisense oligonucleotides for treatment of airway disorders assocd. with bronchoconstriction, lung inflammation, allergies, and surfactant depletion)

IT Emulsions
(oil-in-water; low-adenosine antisense oligonucleotides for treatment of airway disorders assocd. with bronchoconstriction, lung inflammation, allergies, and surfactant depletion)

IT Gene, animal
RL: BOC (Biological occurrence); BSU (Biological study, unclassified); BIOL (Biological study); OCCU (Occurrence)
(oncogene, boundaries of; low-adenosine antisense oligonucleotides for treatment of airway disorders assocd. with bronchoconstriction, lung inflammation, allergies, and surfactant depletion)

IT **Drug delivery systems**
(ophthalmic; low-adenosine antisense oligonucleotides for treatment of airway disorders assocd. with bronchoconstriction, lung inflammation,

allergies, and surfactant depletion)

IT **Drug delivery systems**
(oral; low-adenosine antisense oligonucleotides for treatment of airway disorders assocd. with bronchoconstriction, lung inflammation, allergies, and surfactant depletion)

IT Nervous system
(peripheral, receptors of; low-adenosine antisense oligonucleotides for treatment of airway disorders assocd. with bronchoconstriction, lung inflammation, allergies, and surfactant depletion)

IT Oligonucleotides
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(phosphoramidate; low-adenosine antisense oligonucleotides for treatment of airway disorders assocd. with bronchoconstriction, lung inflammation, allergies, and surfactant depletion)

IT Phosphorothioate oligonucleotides
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(phosphorodithioate; low-adenosine antisense oligonucleotides for treatment of airway disorders assocd. with bronchoconstriction, lung inflammation, allergies, and surfactant depletion)

IT **Drug delivery systems**
(powders; low-adenosine antisense oligonucleotides for treatment of airway disorders assocd. with bronchoconstriction, lung inflammation, allergies, and surfactant depletion)

IT Hypertension
Vasoconstriction
(pulmonary; low-adenosine antisense oligonucleotides for treatment of airway disorders assocd. with bronchoconstriction, lung inflammation, allergies, and surfactant depletion)

IT **Drug delivery systems**
(rectal; low-adenosine antisense oligonucleotides for treatment of airway disorders assocd. with bronchoconstriction, lung inflammation, allergies, and surfactant depletion)

IT **Drug delivery systems**
(slow-release; low-adenosine antisense oligonucleotides for treatment of airway disorders assocd. with bronchoconstriction, lung inflammation, allergies, and surfactant depletion)

IT **Drug delivery systems**
(solns.; low-adenosine antisense oligonucleotides for treatment of airway disorders assocd. with bronchoconstriction, lung inflammation, allergies, and surfactant depletion)

IT **Drug delivery systems**
(sprays; low-adenosine antisense oligonucleotides for treatment of airway disorders assocd. with bronchoconstriction, lung inflammation, allergies, and surfactant depletion)

IT Oligonucleotides
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(sulfonamides; low-adenosine antisense oligonucleotides for treatment of airway disorders assocd. with bronchoconstriction, lung inflammation, allergies, and surfactant depletion)

IT **Drug delivery systems**
(suppositories; low-adenosine antisense oligonucleotides for treatment of airway disorders assocd. with bronchoconstriction, lung inflammation, allergies, and surfactant depletion)

IT **Drug delivery systems**
(suspensions; low-adenosine antisense oligonucleotides for treatment of airway disorders assocd. with bronchoconstriction, lung inflammation, allergies, and surfactant depletion)

IT **Drug delivery systems**
(tablets; low-adenosine antisense oligonucleotides for treatment of airway disorders assocd. with bronchoconstriction, lung inflammation, allergies, and surfactant depletion)

IT Adenosine receptors
Adhesins
Bradykinin receptors
CD34 (antigen)
Chemokine receptors
Chemokines
Cyclophilins
Cytokine receptors
Cytokines
Enzymes, biological studies
Eotaxin
Fibronectins
Growth factors, animal
Histamine receptors
Interleukin 1
Interleukin 1 receptors
Interleukin 11
Interleukin 1.beta.
Interleukin 3 receptors
Interleukin 4 receptors
Interleukin 5 receptors
Interleukin 8 receptors
Interleukin 9
LFA-1 (antigen)
Macrophage inflammatory protein 1.alpha.
Monocyte chemoattractant protein-1
Muscarinic receptors
Neurotransmitters
Prostanoid receptors
RANTES (chemokine)
Receptors
Tachykinin receptors
Transcription factors
Tumor necrosis factors
RL: BOC (Biological occurrence); BSU (Biological study, unclassified); BIOL (Biological study); OCCU (Occurrence)
(**targeted**; low-adenosine antisense oligonucleotides for treatment of airway disorders assocd. with bronchoconstriction, lung inflammation, allergies, and surfactant depletion)

IT Interleukin 3
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(**targeted**; low-adenosine antisense oligonucleotides for treatment of airway disorders assocd. with bronchoconstriction, lung inflammation, allergies, and surfactant depletion)

IT Gene, animal
mRNA
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(**targeting** of; low-adenosine antisense oligonucleotides for treatment of airway disorders assocd. with bronchoconstriction, lung inflammation, allergies, and surfactant depletion)

IT Oligonucleotides
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(thioethers; low-adenosine antisense oligonucleotides for treatment of airway disorders assocd. with bronchoconstriction, lung inflammation, allergies, and surfactant depletion)

IT Oligonucleotides

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(thioformacetals; low-adenosine antisense oligonucleotides for treatment of airway disorders assocd. with bronchoconstriction, lung inflammation, allergies, and surfactant depletion)

IT **Drug delivery systems**
(topical; low-adenosine antisense oligonucleotides for treatment of airway disorders assocd. with bronchoconstriction, lung inflammation, allergies, and surfactant depletion)

IT **Drug delivery systems**
(transdermal; low-adenosine antisense oligonucleotides for treatment of airway disorders assocd. with bronchoconstriction, lung inflammation, allergies, and surfactant depletion)

IT Lung
Lung
(transplant, rejection; low-adenosine antisense oligonucleotides for treatment of airway disorders assocd. with bronchoconstriction, lung inflammation, allergies, and surfactant depletion)

IT Antigens
RL: BOC (Biological occurrence); BSU (Biological study, unclassified); BIOL (Biological study); OCCU (Occurrence)
(**tumor**-assocd., **targeted**; low-adenosine antisense oligonucleotides for treatment of airway disorders assocd. with bronchoconstriction, lung inflammation, allergies, and surfactant depletion)

IT Transferrins
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(uptake agent; low-adenosine antisense oligonucleotides for treatment of airway disorders assocd. with bronchoconstriction, lung inflammation, allergies, and surfactant depletion)

IT **Drug delivery systems**
(vaginal; low-adenosine antisense oligonucleotides for treatment of airway disorders assocd. with bronchoconstriction, lung inflammation, allergies, and surfactant depletion)

IT Peptides, biological studies
RL: BOC (Biological occurrence); BSU (Biological study, unclassified); BIOL (Biological study); OCCU (Occurrence)
(vasoactive, **targeted**; low-adenosine antisense oligonucleotides for treatment of airway disorders assocd. with bronchoconstriction, lung inflammation, allergies, and surfactant depletion)

IT Eukaryote (Eukaryotae)
Prokaryote
(vectors; low-adenosine antisense oligonucleotides for treatment of airway disorders assocd. with bronchoconstriction, lung inflammation, allergies, and surfactant depletion)

IT Emulsions
(water-in-oil; low-adenosine antisense oligonucleotides for treatment of airway disorders assocd. with bronchoconstriction, lung inflammation, allergies, and surfactant depletion)

IT Integrins
RL: BOC (Biological occurrence); BSU (Biological study, unclassified); BIOL (Biological study); OCCU (Occurrence)
(.alpha.4.beta.1, **targeted**; low-adenosine antisense oligonucleotides for treatment of airway disorders assocd. with bronchoconstriction, lung inflammation, allergies, and surfactant depletion)

IT Chemokine receptors
RL: MSC (Miscellaneous)
(.beta. chemokine receptor CCR1, **targeted**; low-adenosine antisense oligonucleotides for treatment of airway disorders assocd.

with bronchoconstriction, lung inflammation, allergies, and surfactant depletion)

IT Chemokine receptors
RL: BOC (Biological occurrence); BSU (Biological study, unclassified); BIOL (Biological study); OCCU (Occurrence)
(.beta. chemokine receptor CCR2, **targeted**; low-adenosine antisense oligonucleotides for treatment of airway disorders assocd. with bronchoconstriction, lung inflammation, allergies, and surfactant depletion)

IT Chemokine receptors
RL: MSC (Miscellaneous)
(.beta. chemokine receptor CCR2, **targeted**; low-adenosine antisense oligonucleotides for treatment of airway disorders assocd. with bronchoconstriction, lung inflammation, allergies, and surfactant depletion)

IT Chemokine receptors
RL: MSC (Miscellaneous)
(.beta. chemokine receptor CCR3, **targeted**; low-adenosine antisense oligonucleotides for treatment of airway disorders assocd. with bronchoconstriction, lung inflammation, allergies, and surfactant depletion)

IT Chemokine receptors
RL: BOC (Biological occurrence); BSU (Biological study, unclassified); BIOL (Biological study); OCCU (Occurrence)
(.beta. chemokine receptor CCR4, **targeted**; low-adenosine antisense oligonucleotides for treatment of airway disorders assocd. with bronchoconstriction, lung inflammation, allergies, and surfactant depletion)

IT Chemokine receptors
RL: MSC (Miscellaneous)
(.beta. chemokine receptor CCR5, **targeted**; low-adenosine antisense oligonucleotides for treatment of airway disorders assocd. with bronchoconstriction, lung inflammation, allergies, and surfactant depletion)

IT Chemokines
RL: MSC (Miscellaneous)
(.beta., receptor CCR5, **targeted**; low-adenosine antisense oligonucleotides for treatment of airway disorders assocd. with bronchoconstriction, lung inflammation, allergies, and surfactant depletion)

IT Adrenoceptors
Integrins
RL: BOC (Biological occurrence); BSU (Biological study, unclassified); BIOL (Biological study); OCCU (Occurrence)
(.beta.2, **targeted**; low-adenosine antisense oligonucleotides for treatment of airway disorders assocd. with bronchoconstriction, lung inflammation, allergies, and surfactant depletion)

IT 59865-13-3, Cyclosporin a
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(**-binding** proteins; low-adenosine antisense oligonucleotides for treatment of airway disorders assocd. with bronchoconstriction, lung inflammation, allergies, and surfactant depletion)

IT 222301-52-2
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(3083; low-adenosine antisense oligonucleotides for treatment of airway disorders assocd. with bronchoconstriction, lung inflammation, allergies, and surfactant depletion)

IT 303816-69-5 303817-26-7 303817-30-3
RL: PRP (Properties)
(Unclaimed; low adenosine anti-sense oligonucleotide, compns., kit and method for treatment of airway disorders assocd. with bronchoconstriction, lung inflammation, allergy(ies) and surfactant depletion)

IT 186470-20-2P 186470-21-3P 186470-22-4P 186676-07-3P 186676-08-4P
186676-09-5P 222186-91-6P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PEP (Physical, engineering or chemical process); PNU (Preparation, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); PROC (Process); USES (Uses)
(antisense to adenosine A1 receptor; low-adenosine antisense oligonucleotides for treatment of airway disorders assocd. with bronchoconstriction, lung inflammation, allergies, and surfactant depletion)

IT 222186-96-1P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PEP (Physical, engineering or chemical process); PNU (Preparation, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); PROC (Process); USES (Uses)
(antisense to adenosine A2b receptor; low-adenosine antisense oligonucleotides for treatment of airway disorders assocd. with bronchoconstriction, lung inflammation, allergies, and surfactant depletion)

IT 222186-93-8P 222186-95-0P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PEP (Physical, engineering or chemical process); PNU (Preparation, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); PROC (Process); USES (Uses)
(antisense to adenosine A3 receptor; low-adenosine antisense oligonucleotides for treatment of airway disorders assocd. with bronchoconstriction, lung inflammation, allergies, and surfactant depletion)

IT 222296-45-9 222405-43-8 222405-45-0
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(control; low-adenosine antisense oligonucleotides for treatment of airway disorders assocd. with bronchoconstriction, lung inflammation, allergies, and surfactant depletion)

IT 125978-95-2, Nitric oxide synthase
RL: BOC (Biological occurrence); BSU (Biological study, unclassified); BIOL (Biological study); OCCU (Occurrence)
(inducible, **targeted**; low-adenosine antisense oligonucleotides for treatment of airway disorders assocd. with bronchoconstriction, lung inflammation, allergies, and surfactant depletion)

IT 58-08-2, Caffeine, biological studies 58-55-9, Theophylline, biological studies 69-89-6, Xanthine 479-18-5, Dyphylline 519-37-9, Etophylline 652-37-9, Acephylline 890-38-0, 2'-Deoxyinosine 2016-63-9, Bamifylline 4546-68-3, 2'-Deoxynebularine 6146-52-7, 5-Nitroindole 41078-02-8, Enprofylline 60254-48-0 126128-35-6 157066-48-3 191421-10-0
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PEP (Physical, engineering or chemical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(low-adenosine antisense oligonucleotides for treatment of airway disorders assocd. with bronchoconstriction, lung inflammation, allergies, and surfactant depletion)

IT 58-61-7, Adenosine, biological studies
RL: BOC (Biological occurrence); BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); OCCU (Occurrence); PROC (Process)
(low-adenosine antisense oligonucleotides for treatment of airway disorders assocd. with bronchoconstriction, lung inflammation, allergies, and surfactant depletion)

IT 103220-14-0, Defensin
RL: BOC (Biological occurrence); BSU (Biological study, unclassified); BIOL (Biological study); OCCU (Occurrence)
(low-adenosine antisense oligonucleotides for treatment of airway disorders assocd. with bronchoconstriction, lung inflammation,

allergies, and surfactant depletion)

IT 150859-22-6 151280-39-6 152920-59-7 158492-48-9 186556-26-3
186556-27-4 186556-28-5 186556-29-6 186556-30-9 186556-31-0
186556-33-2 186556-34-3 186556-35-4 186556-36-5 186556-37-6
186556-39-8 186556-40-1 186556-41-2 186556-42-3 186556-43-4
186556-44-5 186556-45-6 186556-46-7 186556-47-8 186556-48-9
186556-49-0 186556-50-3 186556-51-4 186556-52-5 186619-38-5
186619-39-6 191525-64-1 208884-01-9 222024-49-9 222024-50-2
222024-51-3 222024-52-4 222024-53-5 222024-54-6 222024-55-7
222024-56-8 222024-57-9 222024-60-4 222024-63-7 222024-64-8
222024-65-9 222024-66-0 222024-67-1 222024-69-3 222024-71-7
222024-72-8 222024-73-9 222024-74-0 222024-75-1 222024-76-2
222024-77-3 222024-78-4 222024-79-5 222024-80-8 222024-81-9
222024-83-1 222024-84-2 222024-85-3 222024-86-4 222024-87-5
222024-88-6 222024-89-7 222024-90-0 222024-91-1 222024-92-2
222024-93-3 222024-94-4 222024-95-5 222024-96-6 222024-97-7
222025-02-7 222025-03-8 222025-04-9 222025-05-0 222025-06-1
222025-07-2 222025-08-3 222025-09-4 222025-10-7 222025-11-8
222025-12-9 222025-13-0 222025-14-1 222025-15-2 222025-16-3
222025-17-4 222025-18-5 222025-19-6 222025-21-0 222025-23-2
222025-30-1 222025-33-4 222025-35-6 222025-38-9 222025-39-0
222025-40-3 222025-41-4 222025-42-5 222025-43-6 222025-44-7
222025-45-8 222025-46-9 222025-47-0 222025-48-1 222025-49-2
222025-52-7 222025-53-8 222025-54-9 222025-55-0 222025-56-1
222025-57-2 222025-58-3 222025-59-4 222025-60-7 222025-61-8
222025-62-9 222025-63-0 222025-64-1 222025-65-2 222025-66-3
222025-67-4 222025-68-5 222025-69-6 222025-70-9 222025-71-0
222025-72-1 222025-73-2 222025-75-4 222025-77-6 222025-78-7
222025-79-8 222025-80-1 222025-83-4 222025-86-7 222025-87-8
222025-88-9 222025-89-0 222025-90-3 222025-91-4 222025-92-5
222026-02-0 222026-03-1 222026-07-5 222026-09-7 222026-13-3
222026-18-8 222026-19-9 222026-20-2 222026-21-3 222026-22-4
222026-23-5 222026-24-6 222026-25-7 222026-26-8 222026-27-9
222026-31-5 222026-32-6 222026-33-7 222026-34-8 222026-37-1
222026-40-6 222026-42-8 222026-45-1 222026-47-3 222026-51-9
222026-54-2 222026-57-5 222026-59-7 222026-64-4 222026-65-5
222026-66-6 222026-67-7 222026-68-8 222026-69-9 222026-70-2
222026-72-4 222026-74-6 222026-75-7 222026-77-9 222026-79-1
222026-80-4 222026-82-6 222026-83-7 222026-84-8 222026-85-9
222026-86-0 222026-87-1 222026-88-2 222026-90-6 222026-92-8
222026-94-0 222026-96-2 222026-98-4 222027-01-2 222027-04-5
222027-05-6 222027-07-8 222027-10-3 222027-24-9 222027-27-2
222027-30-7 222027-32-9 222027-34-1 222027-36-3 222027-38-5
222027-41-0 222027-43-2 222027-45-4 222027-47-6 222027-48-7
222027-49-8 222027-50-1 222027-51-2 222027-53-4 222027-55-6
222027-57-8 222027-60-3 222027-61-4 222027-62-5 222027-63-6
222027-64-7 222028-22-0 222028-24-2 222028-26-4 222028-27-5
222028-28-6 222028-29-7 222028-30-0 222028-31-1 222028-39-9
222028-42-4 222028-45-7 222028-47-9

RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(low-adenosine antisense oligonucleotides for treatment of airway disorders assocd. with bronchoconstriction, lung inflammation, allergies, and surfactant depletion)

IT 222028-51-5 222028-52-6 222028-53-7 222028-54-8 222028-55-9
222028-56-0 222028-57-1 222028-60-6 222028-62-8 222028-63-9
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RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(low-adenosine antisense oligonucleotides for treatment of airway disorders assocd. with bronchoconstriction, lung inflammation, allergies, and surfactant depletion)

IT 222031-80-3 222031-81-4 222031-82-5 222031-83-6 222031-86-9
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RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
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RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(low-adenosine antisense oligonucleotides for treatment of airway disorders assocd. with bronchoconstriction, lung inflammation, allergies, and surfactant depletion)

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RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(low-adenosine antisense oligonucleotides for treatment of airway disorders assocd. with bronchoconstriction, lung inflammation, allergies, and surfactant depletion)

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222181-89-7 222181-92-2 222181-93-3
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(low-adenosine antisense oligonucleotides for treatment of airway disorders assocd. with bronchoconstriction, lung inflammation, allergies, and surfactant depletion)

IT 222181-95-5 222181-97-7 222181-98-8 222181-99-9 222182-00-5
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RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(low-adenosine antisense oligonucleotides for treatment of airway disorders assocd. with bronchoconstriction, lung inflammation, allergies, and surfactant depletion)

IT 222301-39-5 222301-42-0 222301-45-3 222301-48-6 222301-49-7
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RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(low-adenosine antisense oligonucleotides for treatment of airway disorders assocd. with bronchoconstriction, lung inflammation, allergies, and surfactant depletion)

IT 222309-50-4 222309-52-6 222309-53-7 222309-54-8 222309-55-9
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RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(low-adenosine antisense oligonucleotides for treatment of airway disorders assocd. with bronchoconstriction, lung inflammation, allergies, and surfactant depletion)

IT 259518-92-8 259518-93-9 259518-94-0 259518-95-1 259518-96-2
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304675-88-5 325605-52-5
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(low-adenosine antisense oligonucleotides for treatment of airway disorders assocd. with bronchoconstriction, lung inflammation, allergies, and surfactant depletion)

IT 84843-69-6, Tryptose
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(receptor, **targeted**; low-adenosine antisense oligonucleotides for treatment of airway disorders assocd. with bronchoconstriction, lung inflammation, allergies, and surfactant depletion)

IT 9004-06-2, Neutrophil elastase 9036-21-9, Phosphodiesterase IV
33507-63-0, Substance p 39391-18-9, Cyclooxygenase 56626-18-7,
Fucosyltransferase 65154-06-5, Paf 71160-24-2, Ltb-4 80619-02-9,
5-Lipoxygenase 81669-70-7, Metalloproteinase 97501-92-3, Chymase
97501-93-4, Tryptase 106096-93-9, Basic fibroblast growth factor
114540-95-3, Preproendothelin 122653-71-8, .beta.2-Adrenergic receptor

kinase 141436-78-4, Protein kinase c
RL: BOC (Biological occurrence); BSU (Biological study, unclassified); BIOL (Biological study); OCCU (Occurrence)
(**targeted**; low-adenosine antisense oligonucleotides for treatment of airway disorders assocd. with bronchoconstriction, lung inflammation, allergies, and surfactant depletion)

IT 131464-24-9 134093-86-0, DNA (human clone 1E11 sialoglycoprotein **VCAM** 1b cDNA) 134195-79-2 134711-87-8 134711-92-5
134802-79-2 135059-92-6 135639-93-9 136046-25-8 139661-10-2
139804-91-4 139805-27-9, GenBank M30510 139805-49-5 139805-50-8
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139837-57-3 139842-20-9, GenBank X54297 139842-21-0 139844-04-5
139848-39-8 139857-92-4 139858-71-2 139868-76-1 139868-86-3
139898-85-4 140026-70-6, GenBank M12807 140027-34-5 140029-01-2, GenBank X14346 140029-22-7, GenBank M15059 140029-23-8 140029-30-7
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140031-94-3 140032-21-9 140032-22-0 140032-24-2 140032-29-7
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140034-13-5, GenBank X07109 140034-18-0 140035-51-4 140036-44-8
140046-39-5 140066-13-3 140066-14-4, GenBank M24283 140070-37-7
140070-47-9 140079-09-0 140079-10-3 140084-30-6 140092-15-5
140092-58-6 140094-50-4 140094-87-7, GenBank X62532 140097-41-2
140098-51-7 140109-60-0 140109-61-1 140109-63-3, DNA (human blood platelet-activating factor receptor gene plus flanks) 140275-92-9
140276-02-4, GenBank M65134 140277-27-6 140277-69-6, GenBank X15161
140277-88-9 140277-89-0 140277-90-3 140278-10-0 140280-37-1
140280-38-2, GenBank X15606 140281-68-1 140281-71-6, GenBank M14098
140281-72-7, GenBank M10322 140281-75-0, GenBank X03131 140281-78-3
140281-79-4, GenBank M22111 140281-80-7, GenBank M29150 140281-81-8, GenBank M54894 140282-11-7 140282-47-9 140282-64-0 140282-70-8
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140288-01-3 140304-67-2 140306-02-1 140316-98-9 140317-07-3
140325-02-6 140325-03-7 140325-14-0 140327-21-5, GenBank X52425
140332-12-3 140332-67-8 140333-25-1 140333-44-4 140337-45-7
140338-87-0, DNA (human gene CMA1 plus flanks) 140339-63-5
140343-92-6, DNA (human tachykinin NK1 receptor cDNA plus 3'-flank)
140344-61-2 140351-10-6 140358-46-9 140508-22-1 140508-44-7
140508-60-7 140509-88-2, GenBank J03049 140513-23-1 140513-71-9
140517-46-0 140555-72-2 140572-85-6 140580-34-3 140742-78-5
140742-82-1, GenBank X02761 140742-91-2 140743-16-4 140744-83-8
140744-85-0, GenBank K02056 140746-31-2, GenBank Y00477 140773-93-9, GenBank M23442 140776-11-0 140794-51-0 140828-40-6 140960-10-7
140983-66-0 141005-40-5 141009-47-4 141162-79-0 141163-56-6, GenBank X62904 141166-97-4 141166-98-5, GenBank X65177 141166-99-6
141167-00-2 141167-01-3 141373-11-7 141705-34-2 141878-70-8
141907-88-2 142098-28-0 142456-15-3, DNA (mouse strain A/J interleukin 10 gene plus flanks) 142463-87-4 142480-83-9, GenBank D10022
142481-89-8 142693-47-8, DNA (human interleukin 11 gene plus flanks)
142788-98-5 142883-18-9 142964-97-4, DNA (human high affinity Fc receptor E .beta.-chain gene plus flanks) 143003-05-8 143003-27-4
143274-62-8 143274-67-3 143342-42-1 143368-90-5 143461-89-6
143461-90-9 143506-54-1 143750-48-5 143845-24-3 143899-74-5
144014-65-3 145281-49-8 145281-50-1 145495-53-0 145598-73-8
145675-58-7, GenBank D10088 145885-74-1 145885-76-3 147401-78-3
147534-25-6 147573-76-0 147845-48-5, DNA (human clone 4.2 gene Tnfa plus gene Tnfb plus flanks) 147904-29-8 148009-68-1, DNA (human clone A10 interleukin 13 cDNA plus flanks) 148107-82-8 148108-33-2, GenBank Y00093 148108-41-2 148283-84-5, DNA (human lung WI-38 cell defensin isoform HNP-3 gene plus flanks) 148284-15-5 148544-84-7 148803-11-6
148955-18-4 148955-19-5 149200-24-8 149426-54-0 149975-08-6,

GenBank Z22804 150219-71-9 150219-87-7, DNA (human clone 210B interleukin 14 cDNA plus flanks) 150246-86-9 150421-31-1, DNA (human protein kinase C isoenzyme .zeta. cDNA) 150511-56-1 150863-54-0, DNA (human interleukin 3 gene 5'-flank) 151151-15-4 151178-54-0, GenBank U00781 151178-55-1, GenBank U00782 151178-56-2, GenBank U00783 151178-58-4, GenBank U00785 151178-59-5, GenBank U00786 151178-60-8, GenBank U00787 151178-61-9, GenBank U00788 151178-80-2, GenBank U00777 151178-81-3, GenBank U00778 151178-82-4, GenBank U00779 151178-83-5, GenBank U00780 151280-40-9, GenBank X68486 151280-41-0 151576-50-0 151576-52-2 151576-86-2 152281-21-5 152283-09-5 152409-22-8 152472-35-0 152472-36-1 152472-37-2 153056-40-7 153270-02-1
RL: PRP (Properties)
(unclaimed nucleotide sequence; low adenosine anti-sense oligonucleotide, compns., kit and method for treatment of airway disorders assocd. with bronchoconstriction, lung inflammation, allergy(ies) and surfactant depletion)

IT 153420-84-9 153420-85-0 153518-32-2 153638-39-2 154997-81-6
155120-05-1 155458-24-5 155459-30-6 155610-25-6 155748-20-2
156253-68-8 156561-36-3 156678-85-2 156794-13-7, GenBank Z22521
156828-74-9 157111-95-0 157114-64-2 157317-36-7, GenBank D10495
157883-58-4 158058-60-7 158082-64-5 158763-39-4 158795-53-0
160121-99-3 160122-00-9 160122-03-2 160122-04-3 160122-05-4
160122-06-5 160122-07-6 160122-08-7 160122-09-8 160122-10-1
160122-11-2 160122-13-4 160122-14-5 160122-15-6 160122-47-4
160122-48-5 160122-49-6 160122-50-9 160122-51-0 160122-52-1
160122-53-2 160122-54-3 160122-55-4 160122-56-5 162162-39-2
162198-08-5 163474-09-7 165763-93-9 166424-71-1 166840-83-1
166924-64-7 167712-04-1 167712-05-2 167713-64-6 167714-05-8
168309-43-1 168309-44-2 168385-31-7 168663-08-9 169022-12-2
169022-13-3 169278-01-7 169278-02-8 169278-03-9 169278-09-5
169278-10-8 169716-15-8 170274-34-7 171751-94-3 173707-28-3, DNA (human clone 25 eotaxin cDNA) 174057-08-0 174253-61-3 174253-63-5
174253-66-8 174253-68-0 174253-69-1 174253-71-5 175109-39-4
176145-60-1 176630-35-6 176667-27-9 177256-95-0 177301-96-1
177308-40-6 177308-41-7 177308-45-1 177891-71-3 177891-86-0
178858-57-6 179378-35-9 179725-94-1 180884-23-5 181726-26-1
182094-87-7 183640-70-2 183976-80-9 184383-54-8 184517-66-6
184754-45-8 185077-28-5 185773-11-9 186227-94-1 186227-95-2
186227-96-3 186918-23-0 186985-07-9 187353-98-6 187859-79-6
189236-80-4 189327-88-6 190146-48-6 190305-70-5 190550-91-5
190894-25-8 191303-39-6 191303-40-9 191303-41-0 191303-42-1
191303-43-2 191525-65-2 191525-66-3 192736-48-4 192738-08-2
194899-62-2 199410-24-7 199413-04-2 200077-73-2 200158-82-3
200366-91-2 200591-72-6 201952-11-6 202944-00-1 205287-23-6
206219-72-9 207943-79-1 212277-59-3 215917-28-5 218268-17-8
218268-18-9 218268-19-0 218268-20-3 219100-45-5 220279-04-9, DNA (human gene IL7R exon 1 plus flanks) 220629-39-0 220629-40-3
220629-41-4 220629-42-5 220693-06-1 222297-53-2 223656-93-7
223656-94-8 225253-03-2 225253-04-3 252550-99-5 252693-25-7
252697-89-5 252698-63-8 252699-61-9 252775-20-5 252775-21-6
252775-22-7 252775-23-8 252775-24-9 252783-26-9 252796-58-0
259647-94-4 259648-00-5 259648-06-1 259724-09-9 259724-23-7
260022-59-1 260022-60-4 260022-72-8 260022-74-0 260022-75-1
260022-77-3 260022-81-9 260022-82-0 260022-83-1 260022-84-2
260022-86-4 260022-87-5 260022-88-6 260022-89-7 260022-91-1
260022-93-3 260022-95-5 303816-05-9 303816-06-0 303816-07-1
303816-08-2 303816-09-3 303816-10-6 303816-11-7 303816-12-8
303816-13-9 303816-14-0 303816-15-1 303816-16-2 303816-17-3
303816-18-4 303816-19-5 303816-20-8 303816-21-9 303816-22-0
303816-23-1 303816-24-2 303816-25-3 303816-26-4 303816-27-5
303816-28-6 303816-29-7 303816-30-0 303816-31-1 303816-32-2
303816-33-3 303816-34-4 303816-35-5 303816-36-6 303816-37-7
303816-38-8 303816-39-9 303816-40-2 303816-41-3 303816-54-8

303816-55-9 303816-56-0 303816-57-1 303816-58-2 303816-60-6
303816-61-7 303816-62-8 303816-63-9 303816-64-0 303816-65-1
303816-66-2 303816-67-3
RL: PRP (Properties)
(unclaimed nucleotide sequence; low adenosine anti-sense oligonucleotide, compns., kit and method for treatment of airway disorders assocd. with bronchoconstriction, lung inflammation, allergy(ies) and surfactant depletion)

IT 303816-68-4 303816-70-8 303816-71-9 303816-72-0 303816-73-1
303816-74-2 303816-75-3 303816-76-4 303816-77-5 303816-78-6
303816-79-7 303816-80-0 303816-81-1 303816-82-2 303816-83-3
303816-84-4 303816-85-5 303816-86-6 303816-87-7 303816-88-8
303816-89-9 303816-90-2 303816-91-3 303816-92-4 303816-93-5
303816-94-6 303816-95-7 303816-96-8 303816-97-9 303816-98-0
303816-99-1 303817-00-7 303817-01-8 303817-04-1 303817-05-2
303817-06-3 303817-07-4 303817-08-5 303817-09-6 303817-10-9
303817-11-0 303817-12-1 303817-13-2 303817-14-3 303817-15-4
303817-16-5 303817-17-6 303817-18-7 303817-19-8 303817-20-1
303817-21-2 303817-22-3 303817-23-4 303817-24-5 303817-25-6
303817-27-8 303817-28-9 303817-29-0 303817-31-4 303817-32-5
303817-33-6 303817-34-7 303817-35-8 303817-36-9 303817-37-0
303817-38-1 303817-39-2 303817-40-5
RL: PRP (Properties)
(unclaimed nucleotide sequence; low adenosine anti-sense oligonucleotide, compns., kit and method for treatment of airway disorders assocd. with bronchoconstriction, lung inflammation, allergy(ies) and surfactant depletion)

IT 303816-59-3
RL: PRP (Properties)
(unclaimed sequence; low adenosine anti-sense oligonucleotide, compns., kit and method for treatment of airway disorders assocd. with bronchoconstriction, lung inflammation, allergy(ies) and surfactant depletion)

IT 9013-20-1, Streptavidin
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(uptake agent; low-adenosine antisense oligonucleotides for treatment of airway disorders assocd. with bronchoconstriction, lung inflammation, allergies, and surfactant depletion)

L56 ANSWER 9 OF 15 HCAPLUS COPYRIGHT 2002 ACS
AN **2000:133697** HCAPLUS
DN **132:203144**
TI Low-adenosine antisense oligonucleotide agents, compositions, kits and treatments for respiratory disorders
IN Nyce, Jonathan W.
PA East Carolina University, USA
SO PCT Int. Appl., 1343 pp.
CODEN: PIXXD2
DT Patent
LA English
IC ICM C07H
CC 1-9 (Pharmacology)
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2000009525	A2	20000224	WO 1999-US17712	19990803
	WO 2000009525	A3	20000518		
	W: AU, CA, CN, MX, RU, US				
	RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
	AU 9953374	A1	20000306	AU 1999-53374	19990803
	EP 1102786	A2	20010530	EP 1999-939006	19990803

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI

PRAI US 1998-95212P P 19980803
WO 1999-US17712 W 19990803

OS MARPAT 132:203144

AB A compn. comprises a nucleic acid comprising an oligo antisense to a **target** such as polypeptide(s) assocd. with an ailment afflicting lung airways, genes and mRNAs encoding them, genomic and mRNA flanking regions, intron and exon borders and all regulatory and functionally related segments of the genes and mRNAs encoding the polypeptides, their salts and mixts. Various formulations contain a requisite **carrier**, and optionally other additives and biol. active agents. The agent of the invention may be prepd. by selecting a **target** gene(s), genomic flanking region(s), RNA(s) and/or polypeptide(s) assocd. with a disease(s) or condition(s) afflicting lung airways, obtaining the sequence of the mRNA(s) corresponding to the **target** gene(s) and/or genomic flanking region(s), and/or RNAs encoding the **target** polypeptide(s), selecting at least one segment of the mRNA which may be up to 60% free of thymidine (T) and synthesizing one or more antisense oligonucleotide(s) to the mRNA segments which are free of adenosine (A) by substituting a universal base for A when present in the oligonucleotide. The agent may be prepd. by selection of **target** nucleic acid sequences with GC running stretches, which have low T content, and by optionally replacing A in the antisense oligonucleotides with a universal base. The agent, compn. and formulations are used for prophylactic, preventive and therapeutic treatment of ailments assocd. with impaired respiration, allergy(ies) and/or inflammation, such as pulmonary vasoconstriction, inflammation, allergies, asthma, impeded respiration, lung pain, cystic fibrosis, bronchoconstriction, pulmonary hypertension and bronchoconstriction, chronic bronchitis, emphysema, chronic obstructive pulmonary disease (COPD), acute respiratory distress syndrome (ARDS), ischemic conditions including ischemia itself, and **cancers** such as leukemias, lymphomas, **carcinomas**, and the like, e.g. colon **cancer**, breast **cancer**, pancreatic **cancer**, lung **cancer**, hepatocellular **carcinoma**, kidney **cancer**, **melanoma**, hepatic **metastasis**, etc., as well as all types of **cancers** with may **metastasize** or have **metastasized** to the lung(s), including breast and prostate **cancer**. The present treatment is suitable for administration in combination with other treatments, e.g. before, during and after other treatments, including **radiation**, **chemotherapy**, **antibody** therapy and surgery, among others. The present agent is effectively administered preventatively, prophylactically or therapeutically by itself for conditions without known therapies, or as a substitute for, or in conjunction with, other therapies exhibiting undesirable side effects. The treatment of this invention may be administered directly into the respiratory system of a subject, so that the agent has direct access to the airways and the lungs. The invention is exemplified with specificity and pharmacokinetic studies using phosphorothioated antisense oligonucleotides **targeted** to the adenosine receptors A1, A2a, A2b, and A3.

ST antisense oligonucleotide respiratory disorder; lung airway obstruction antisense oligonucleotide; asthma treatment antisense oligonucleotide; inflammation treatment antisense oligonucleotide; allergy treatment antisense oligonucleotide; **cancer** treatment antisense oligonucleotide

IT Transcription factors
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(AP-1 (activator protein 1), **target**; low-adenosine antisense oligonucleotide agents, compns., kits and treatments for respiratory disorders)

IT Adenosine receptors

RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(A1, **target**; low-adenosine antisense oligonucleotide agents, compns., kits and treatments for respiratory disorders)

IT Purinoceptor agonists
Purinoceptor antagonists
(A1; low-adenosine antisense oligonucleotide agents, compns., kits and treatments for respiratory disorders)

IT Purinoceptor agonists
Purinoceptor antagonists
(A2; low-adenosine antisense oligonucleotide agents, compns., kits and treatments for respiratory disorders)

IT Adenosine receptors
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(A2A, **target**; low-adenosine antisense oligonucleotide agents, compns., kits and treatments for respiratory disorders)

IT Adenosine receptors
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(A2B, **target**; low-adenosine antisense oligonucleotide agents, compns., kits and treatments for respiratory disorders)

IT Adenosine receptors
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(A3, **target**; low-adenosine antisense oligonucleotide agents, compns., kits and treatments for respiratory disorders)

IT Bradykinin receptors
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(B2, **target**; low-adenosine antisense oligonucleotide agents, compns., kits and treatments for respiratory disorders)

IT Chemokines
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(C-C, receptors, CCR3, **target**; low-adenosine antisense oligonucleotide agents, compns., kits and treatments for respiratory disorders)

IT Chemokines
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(C-C, .beta., receptor CCR2, **target**; low-adenosine antisense oligonucleotide agents, compns., kits and treatments for respiratory disorders)

IT Diglycerides
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(CDP-deriv., surfactant for **drug delivery**; low-adenosine antisense oligonucleotide agents, compns., kits and treatments for respiratory disorders)

IT **Selectins**
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(**E-**, **target**; low-adenosine antisense oligonucleotide agents, compns., kits and treatments for respiratory disorders)

IT **Endothelin** receptors
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(ETA, **target**; low-adenosine antisense oligonucleotide agents, compns., kits and treatments for respiratory disorders)

IT **Endothelin** receptors
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)

(ETB, **target**; low-adenosine antisense oligonucleotide agents, compns., kits and treatments for respiratory disorders)

IT Proteins, specific or class
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(FKBP (FK 506-**binding** protein), **target**; low-adenosine antisense oligonucleotide agents, compns., kits and treatments for respiratory disorders)

IT Transcription factors
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(GATA-3, **target**; low-adenosine antisense oligonucleotide agents, compns., kits and treatments for respiratory disorders)

IT **Cell adhesion molecules**
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(**ICAM-1** (**intercellular adhesion mol. 1**), **target**; low-adenosine antisense oligonucleotide agents, compns., kits and treatments for respiratory disorders)

IT **Cell adhesion molecules**
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(**ICAM**-2 (**intercellular adhesion mol.** 2), **target**; low-adenosine antisense oligonucleotide agents, compns., kits and treatments for respiratory disorders)

IT **Cell adhesion molecules**
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(**ICAM**-3 (**intercellular adhesion mol.** 3), **target**; low-adenosine antisense oligonucleotide agents, compns., kits and treatments for respiratory disorders)

IT Immunoglobulin receptors
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(IgE, **target**; low-adenosine antisense oligonucleotide agents, compns., kits and treatments for respiratory disorders)

IT **Selectins**
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(L-, **target**; low-adenosine antisense oligonucleotide agents, compns., kits and treatments for respiratory disorders)

IT Integrins
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(LPAM-1 (lymphocyte Peyer's patch high **endothelial** venule **adhesion** mol. 1), **target**; low-adenosine antisense oligonucleotide agents, compns., kits and treatments for respiratory disorders)

IT Cytokines
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(MBP (major basic protein), **target**; low-adenosine antisense oligonucleotide agents, compns., kits and treatments for respiratory disorders)

IT Transcription factors
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(NF-IL6 (nuclear factor interleukin 6), **target**; low-adenosine antisense oligonucleotide agents, compns., kits and treatments for respiratory disorders)

IT Transcription factors
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(NF-.kappa.B (nuclear factor .kappa.B), **target**; low-adenosine antisense oligonucleotide agents, compns., kits and treatments for respiratory disorders)

IT Transcription factors
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(NFAT-1 (nuclear factor, activated T-cell, 1), **target**; low-adenosine antisense oligonucleotide agents, compns., kits and treatments for respiratory disorders)

IT Tachykinin receptors
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(NK1, **target**; low-adenosine antisense oligonucleotide agents, compns., kits and treatments for respiratory disorders)

IT **Selectins**
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(**P-**, **target**; low-adenosine antisense oligonucleotide agents, compns., kits and treatments for respiratory disorders)

IT **Cell adhesion molecules**
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(**PECAM-1**, **target**; low-adenosine antisense oligonucleotide agents, compns., kits and treatments for respiratory disorders)

IT Glycoproteins, specific or class
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(PSGL-1 (**P-selectin** glycoprotein ligand-1), **target**; low-adenosine antisense oligonucleotide agents, compns., kits and treatments for respiratory disorders)

IT Surfactant proteins (pulmonary)
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(SP-A, surfactant for **drug delivery**; low-adenosine antisense oligonucleotide agents, compns., kits and treatments for respiratory disorders)

IT Surfactant proteins (pulmonary)
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(SP-B, surfactant for **drug delivery**; low-adenosine antisense oligonucleotide agents, compns., kits and treatments for respiratory disorders)

IT Surfactant proteins (pulmonary)
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(SP-C, surfactant for **drug delivery**; low-adenosine antisense oligonucleotide agents, compns., kits and treatments for respiratory disorders)

IT Surfactant proteins (pulmonary)
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(SP-D, surfactant for **drug delivery**; low-adenosine antisense oligonucleotide agents, compns., kits and treatments for respiratory disorders)

IT Transcription factors
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(STAT4, **target**; low-adenosine antisense oligonucleotide agents, compns., kits and treatments for respiratory disorders)

IT **Cell adhesion molecules**
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)

(**VCAM-1**, **target**; low-adenosine antisense oligonucleotide agents, compns., kits and treatments for respiratory disorders)

IT **Drug delivery systems**
(aerosols; low-adenosine antisense oligonucleotide agents, compns., kits and treatments for respiratory disorders)

IT Integrins
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(antigens Mac-1 (macrophage 1), **target**; low-adenosine antisense oligonucleotide agents, compns., kits and treatments for respiratory disorders)

IT Sialoglycoproteins
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(asialoglycoproteins, **drug** uptake enhancer; low-adenosine antisense oligonucleotide agents, compns., kits and treatments for respiratory disorders)

IT Proteins, specific or class
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(**binding**, **target**; low-adenosine antisense oligonucleotide agents, compns., kits and treatments for respiratory disorders)

IT **Drug delivery systems**
(capsules; low-adenosine antisense oligonucleotide agents, compns., kits and treatments for respiratory disorders)

IT Proteins, specific or class
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(cyclosporin A-**binding**, **target**; low-adenosine antisense oligonucleotide agents, compns., kits and treatments for respiratory disorders)

IT Leukotriene receptors
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(cysteine-contg., **target**; low-adenosine antisense oligonucleotide agents, compns., kits and treatments for respiratory disorders)

IT Respiratory tract
(disease, obstructive; low-adenosine antisense oligonucleotide agents, compns., kits and treatments for respiratory disorders)

IT Antioxidants
Buffers
Coloring materials
Dispersing agents
Fillers
Flavoring materials
Preservatives
Propellants (sprays and foams)
Surfactants
(**drug delivery** system contg.; low-adenosine antisense oligonucleotide agents, compns., kits and treatments for respiratory disorders)

IT Ribozymes
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(**drug delivery** system contg.; low-adenosine antisense oligonucleotide agents, compns., kits and treatments for respiratory disorders)

IT Transferrins
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(**drug** uptake enhancer; low-adenosine antisense oligonucleotide agents, compns., kits and treatments for respiratory disorders)

IT **Drug delivery systems**
(emulsions; low-adenosine antisense oligonucleotide agents, compns., kits and treatments for respiratory disorders)

IT Chemokine receptors
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(fusin, **target**; low-adenosine antisense oligonucleotide agents, compns., kits and treatments for respiratory disorders)

IT Proteins, specific or class
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(gene c-mas, **target**; low-adenosine antisense oligonucleotide agents, compns., kits and treatments for respiratory disorders)

IT Interleukin receptors
Interleukin receptors
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(interleukin 11, **target**; low-adenosine antisense oligonucleotide agents, compns., kits and treatments for respiratory disorders)

IT Interleukin 1 receptors
Interleukin 1 receptors
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(interleukin 1.beta., **target**; low-adenosine antisense oligonucleotide agents, compns., kits and treatments for respiratory disorders)

IT Interleukin receptors
Interleukin receptors
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(interleukin 9, **target**; low-adenosine antisense oligonucleotide agents, compns., kits and treatments for respiratory disorders)

IT Leukotriene receptors
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(leukotriene B4, **target**; low-adenosine antisense oligonucleotide agents, compns., kits and treatments for respiratory disorders)

IT **Drug delivery systems**
(**liposomes**; low-adenosine antisense oligonucleotide agents, compns., kits and treatments for respiratory disorders)

IT Allergy inhibitors
Anti-inflammatory agents
Antiasthmatics
Antitumor agents
Bronchodilators
Drug delivery systems
Genetic vectors
Purinoceptor agonists
Purinoceptor antagonists
(low-adenosine antisense oligonucleotide agents, compns., kits and treatments for respiratory disorders)

IT Antisense oligonucleotides
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(low-adenosine antisense oligonucleotide agents, compns., kits and treatments for respiratory disorders)

IT Chemokines
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(monocyte chemoattractant protein 3, **target**; low-adenosine antisense oligonucleotide agents, compns., kits and treatments for

respiratory disorders)

IT Chemokines
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(monocyte chemoattractant protein 4, **target**; low-adenosine antisense oligonucleotide agents, compns., kits and treatments for respiratory disorders)

IT Chemokines
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(monocyte chemoattractant protein-2, **target**; low-adenosine antisense oligonucleotide agents, compns., kits and treatments for respiratory disorders)

IT Lung
(multilamellar body, surfactant for **drug delivery**; low-adenosine antisense oligonucleotide agents, compns., kits and treatments for respiratory disorders)

IT Receptors
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(neutrophil adherence, **target**; low-adenosine antisense oligonucleotide agents, compns., kits and treatments for respiratory disorders)

IT Cytokines
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(neutrophil chemotactic factor, **target**; low-adenosine antisense oligonucleotide agents, compns., kits and treatments for respiratory disorders)

IT Gene, animal
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(oncogene, **target**; low-adenosine antisense oligonucleotide agents, compns., kits and treatments for respiratory disorders)

IT Integrins
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(p150,95 antigen, **target**; low-adenosine antisense oligonucleotide agents, compns., kits and treatments for respiratory disorders)

IT Fatty acids, biological studies
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(polyunsatd., omega-3, surfactant for **drug delivery** ; low-adenosine antisense oligonucleotide agents, compns., kits and treatments for respiratory disorders)

IT **Drug delivery systems**
(sprays; low-adenosine antisense oligonucleotide agents, compns., kits and treatments for respiratory disorders)

IT **Drug delivery systems**
(suppositories; low-adenosine antisense oligonucleotide agents, compns., kits and treatments for respiratory disorders)

IT Phosphatidylglycerols
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(surfactant for **drug delivery** contg.; low-adenosine antisense oligonucleotide agents, compns., kits and treatments for respiratory disorders)

IT Lecithins
Lysophosphatidylcholines
Lysophosphatidylethanolamines
Phosphatidic acids
Phosphatidylcholines, biological studies
Phosphatidylethanolamines, biological studies
Phosphatidylinositols

Phosphatidylserines
Polyoxyalkylenes, biological studies
Sulfatides
Surfactant proteins (pulmonary)
Ubiquinones
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(surfactant for **drug delivery**; low-adenosine antisense oligonucleotide agents, compns., kits and treatments for respiratory disorders)

IT **Drug delivery systems**
(tablets; low-adenosine antisense oligonucleotide agents, compns., kits and treatments for respiratory disorders)

IT CD34 (antigen)
Cell adhesion molecules
Chemokine receptors
Chemokines
Cyclophilins
Enzymes, biological studies
Eotaxin
Fibronectins
Growth factors, animal
Histamine receptors
Immunoglobulin receptors
Immunoglobulins
Interleukin 1
Interleukin 1 receptors
Interleukin 11
Interleukin 1.beta.
Interleukin 3
Interleukin 3 receptors
Interleukin 4 receptors
Interleukin 5 receptors
Interleukin 8 receptors
Interleukin 9
Interleukin receptors
Interleukins
LFA-1 (antigen)
Macrophage inflammatory protein 1.alpha.
Monocyte chemoattractant protein-1
Muscarinic receptors
Neurotransmitters
Prostanoid receptors
RANTES (chemokine)
Receptors
Selectins
Tachykinin receptors
Transcription factors
Tumor necrosis factors
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(**target**; low-adenosine antisense oligonucleotide agents, compns., kits and treatments for respiratory disorders)

IT Receptors
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(tryptose, **target**; low-adenosine antisense oligonucleotide agents, compns., kits and treatments for respiratory disorders)

IT Peptide receptors
Peptides, biological studies
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(vasoactive, **target**; low-adenosine antisense oligonucleotide agents, compns., kits and treatments for respiratory disorders)

IT Integrins
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(.alpha.4.beta.1, **target**; low-adenosine antisense oligonucleotide agents, compns., kits and treatments for respiratory disorders)

IT Chemokine receptors
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(.beta. chemokine receptor CCR3, **target**; low-adenosine antisense oligonucleotide agents, compns., kits and treatments for respiratory disorders)

IT Chemokine receptors
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(.beta. chemokine receptor CCR5, **target**; low-adenosine antisense oligonucleotide agents, compns., kits and treatments for respiratory disorders)

IT Chemokines
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(.beta., receptor CCR5, **target**; low-adenosine antisense oligonucleotide agents, compns., kits and treatments for respiratory disorders)

IT 134195-79-2 134196-06-8 134711-87-8 139497-35-1 139805-27-9, GenBank M30510 139808-13-2 139808-61-0, GenBank M34379 139808-76-7 139817-63-3 139835-11-3 139842-20-9, GenBank X54297 139848-39-8 140026-70-6, GenBank M12807 140029-22-7, GenBank M15059 140029-23-8 140031-24-9 140031-31-8, GenBank K03122 140031-34-1 140031-39-6 140032-29-7 140034-13-5, DNA (human clone H707 cDNA) 140070-37-7 140092-15-5 140094-87-7, GenBank X62532 140109-63-3, DNA (human blood platelet-activating factor receptor gene plus flanks) 140277-69-6, GenBank X15161 140278-10-0 140280-38-2, GenBank X15606 140281-71-6, GenBank M14098 140281-72-7, GenBank M10322 140281-75-0, GenBank X03131 140281-79-4, GenBank M22111 140281-80-7, GenBank M29150 140281-81-8, GenBank M54894 140306-02-1 140318-41-8, GenBank M62424 140325-14-0 140339-63-5 140508-44-7 140509-88-2, GenBank J03049 140555-72-2 140572-85-6 140742-78-5 140746-31-2, GenBank Y00477 140772-35-6, GenBank M26115 141907-88-2 142456-15-3, DNA (mouse strain A/J interleukin 10 gene plus flanks) 142463-87-4 142480-83-9, GenBank D10022 143003-27-4 143845-24-3 144014-65-3 145281-50-1 145675-58-7, GenBank D10088 145885-75-2 145885-76-3 147904-29-8 148009-68-1, DNA (human clone A10 interleukin 13 cDNA plus flanks) 148108-41-2 148803-11-6 150219-87-7, DNA (human clone 210B interleukin 14 cDNA plus flanks) 150421-31-1, DNA (human protein kinase C isoenzyme .zeta. cDNA) 151178-54-0, GenBank U00781 151178-55-1, GenBank U00782 151178-56-2, GenBank U00783 151178-57-3, GenBank U00784 151178-58-4, GenBank U00785 151178-59-5, GenBank U00786 151178-60-8, GenBank U00787 151178-61-9, GenBank U00788 151178-79-9 151178-80-2, GenBank U00777 151178-81-3, GenBank U00778 151178-82-4, GenBank U00779 151178-83-5, GenBank U00780 152281-21-5 152409-22-8 153420-84-9 153420-85-0 155120-05-1 156253-68-8 156561-36-3 156794-13-7, GenBank Z22521 156795-75-4 157317-36-7 158082-64-5 158645-16-0 165763-93-9 167712-04-1 167712-05-2 169015-39-8 169022-13-3 170274-34-7 171751-94-3 176667-27-9 177891-71-3 178097-63-7 185009-07-8, GenBank Z70243 185773-11-9 186163-98-4, GenBank I34195 186918-23-0 187353-98-6 188070-95-3 189327-88-6 190396-89-5 194899-62-2 200077-73-2 200366-91-2 201952-11-6 205287-23-6 206219-72-9 207943-79-1 212277-59-3 220279-04-9, DNA (human gene IL7R exon 1 plus flanks) 224934-71-8, GenBank AE001453 252550-99-5 252690-09-8, GenBank S46030 252693-25-7 252698-63-8 252699-61-9 252775-20-5 252775-21-6 252775-23-8 252775-24-9 260022-99-9
RL: PRP (Properties)

(Unclaimed; low-adenosine antisense oligonucleotide agents, compns., kits and treatments for respiratory disorders)

IT 190894-25-8
RL: PRP (Properties)
(Unclaimed; reglow-adenosine antisense oligonucleotide reagents, compns., kits and treatments for respiratory disorders)

IT 140034-11-3, GenBank M27545 252775-22-7
RL: PRP (Properties)
(Unclaimed; rlow-adenosine antisense oligonucleotide agents, compns., kits and treatments for respiratory disorders)

IT 186470-20-2 186676-07-3 222186-91-6
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(adenosine A1 receptor-specific; low-adenosine antisense oligonucleotide agents, compns., kits and treatments for respiratory disorders)

IT 158492-48-9 208884-01-9 222024-49-9 222024-50-2 222024-51-3
222024-52-4 222024-53-5 222024-54-6 222024-55-7 222024-56-8
222024-57-9 222024-60-4 222024-63-7 222024-64-8 222024-65-9
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222024-73-9 222024-74-0 222024-75-1 222024-76-2 222024-77-3
222024-78-4 222024-79-5 222024-80-8 222024-81-9 222024-83-1
222024-84-2 222024-85-3 222024-86-4 222024-87-5 222024-88-6
222024-89-7 222024-90-0 222024-91-1 222024-92-2 222024-93-3
222024-94-4 222024-95-5 222024-96-6 222024-97-7 222025-02-7
222025-03-8 222025-04-9 222025-05-0 222025-06-1 222025-07-2
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222025-18-5 222025-19-6 222025-21-0 222025-23-2 222025-30-1
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222025-41-4 222025-42-5 222025-43-6 222025-44-7 222025-45-8
222025-46-9 222025-47-0 222025-48-1 222025-49-2 222025-52-7
222025-53-8 222025-54-9 222025-55-0 222025-56-1 222025-57-2
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222025-68-5 222025-69-6 222025-70-9 222025-71-0 222025-72-1
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222028-98-0 222028-99-1 222029-00-7 222029-02-9 222029-04-1
222029-05-2 222029-07-4 222029-08-5
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(adenosine A1 receptor-specific; low-adenosine antisense oligonucleotide agents, compns., kits and treatments for respiratory disorders)

IT 222029-09-6 222029-10-9 222029-11-0 222029-12-1 222029-13-2
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RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(adenosine A1 receptor-specific; low-adenosine antisense oligonucleotide agents, compns., kits and treatments for respiratory disorders)

IT 222034-13-1 222034-14-2 222034-15-3 222034-16-4 222034-17-5
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222038-68-8 222038-69-9 222038-70-2 222038-71-3 222038-72-4
222038-73-5 222038-74-6 222038-75-7 222038-76-8 222038-77-9
222038-78-0 222038-79-1 222038-80-4 222038-82-6 222038-83-7
222038-84-8 222038-85-9 222038-86-0 222038-87-1 222038-88-2
222038-89-3 222038-90-6 222038-91-7 222038-92-8 222038-93-9
222038-94-0 222038-95-1 222038-96-2 222038-97-3 222038-98-4
222038-99-5 222039-00-1 222039-01-2
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(adenosine A1 receptor-specific; low-adenosine antisense
oligonucleotide agents, compns., kits and treatments for respiratory
disorders)

IT 222039-02-3 222039-03-4 222039-04-5 222039-05-6 222039-06-7
222039-08-9 222039-09-0 222039-10-3 222039-11-4 222039-12-5
222039-13-6 222039-15-8 222039-16-9 222039-17-0 222039-18-1
222039-19-2 222039-20-5 222039-21-6 222039-22-7 222039-23-8
222039-24-9 222039-25-0 222039-26-1 222039-27-2 222039-28-3
222039-29-4 222039-30-7 222039-31-8 222039-32-9 222039-33-0
222039-34-1 222039-35-2 222039-36-3 222039-37-4 222039-38-5
222039-39-6 222039-40-9 222039-41-0 222039-42-1 222039-43-2
222039-47-6 222039-48-7 222039-50-1 222039-51-2 222039-52-3
222039-53-4 222039-54-5 222039-55-6 222039-56-7 222039-57-8
222039-58-9 222039-59-0 222039-60-3 222039-61-4 222039-62-5
222039-63-6 222039-64-7 222039-65-8 222039-66-9 222039-67-0
222039-68-1 222039-69-2 222039-70-5 222039-71-6 222039-72-7
222039-73-8 222039-74-9 222039-75-0 222039-76-1 222039-77-2
222039-78-3 222039-79-4 222039-80-7 222039-81-8 222039-82-9
222039-83-0 222039-84-1 222039-85-2 222039-86-3 222039-87-4

222039-88-5 222039-89-6 222039-90-9 222039-91-0 222039-92-1
222039-93-2 222039-94-3 222039-95-4 222039-96-5 222039-97-6
222039-98-7 222039-99-8 222040-00-8 222040-01-9 222040-02-0
222040-03-1 222040-04-2 222040-05-3 222040-06-4 222040-07-5
222040-08-6 222040-09-7 222040-10-0 222040-11-1 222040-12-2
222040-13-3 222040-14-4 222040-15-5 222040-16-6 222040-17-7
222040-18-8 222040-19-9 222040-20-2 222040-21-3 222040-22-4
222040-34-8 222040-37-1 222040-38-2 222040-40-6 222040-41-7
222040-42-8 222040-43-9 222040-44-0 222040-47-3 222040-49-5
222040-50-8 222040-51-9 222040-53-1 222040-54-2 222040-55-3
222040-56-4 222040-57-5 222040-58-6 222040-59-7 222040-60-0
222040-61-1 222040-62-2 222040-63-3 222040-64-4 222040-65-5
222040-66-6 222040-67-7 222040-68-8 222040-69-9 222040-70-2
222040-71-3 222040-72-4 222040-73-5 222040-74-6 222040-75-7
222040-76-8 222040-77-9 222040-78-0 222040-79-1 222040-80-4
222040-81-5 222040-82-6 222040-84-8 222040-85-9 222040-86-0
222040-88-2 222040-89-3 222040-91-7 222040-93-9 222040-95-1
222040-97-3 222040-99-5 222041-00-1 222041-01-2 222041-02-3
222041-03-4 222041-06-7 222041-09-0 222041-14-7 222186-46-1
222186-54-1 222186-55-2 222186-60-9 222186-63-2 222186-71-2
222186-73-4 222186-74-5 222186-75-6 222186-76-7 222186-81-4
222186-82-5 222186-83-6 222186-84-7 222186-86-9 222186-87-0
222186-89-2 222533-35-9 325605-52-5
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(adenosine A1 receptor-specific; low-adenosine antisense oligonucleotide agents, compns., kits and treatments for respiratory disorders)

IT 222186-96-1
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(adenosine A2b receptor-specific; low-adenosine antisense oligonucleotide agents, compns., kits and treatments for respiratory disorders)

IT 186556-27-4 222041-47-6 222041-48-7 222041-49-8 222041-50-1
222041-51-2 222041-52-3 222041-53-4 222041-54-5
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(adenosine A2b receptor-specific; low-adenosine antisense oligonucleotide agents, compns., kits and treatments for respiratory disorders)

IT 186556-26-3 222041-34-1 222041-35-2 222041-36-3 222041-37-4
222041-38-5 222041-39-6 222041-40-9 222041-41-0 222041-42-1
222041-43-2 222041-44-3 222041-45-4 222041-46-5
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(adenosine A2a receptor-specific; low-adenosine antisense oligonucleotide agents, compns., kits and treatments for respiratory disorders)

IT 186470-21-3 186470-22-4 186676-08-4 186676-09-5 222186-93-8
222186-95-0
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(adenosine A3 receptor-specific; low-adenosine antisense oligonucleotide agents, compns., kits and treatments for respiratory disorders)

IT 222041-56-7 222041-57-8 222041-58-9 222041-59-0 222041-60-3
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(adenosine A3 receptor-specific; low-adenosine antisense oligonucleotide agents, compns., kits and treatments for respiratory disorders)

IT 9013-20-1, Streptavidin
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(**drug** uptake enhancer; low-adenosine antisense

oligonucleotide agents, compns., kits and treatments for respiratory disorders)

IT 186556-37-6 222174-68-7 222174-69-8 222174-70-1 222174-73-4
259239-95-7
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(human ELAM-1-specific; low-adenosine antisense oligonucleotide agents, compns., kits and treatments for respiratory disorders)

IT 186619-38-5 222041-64-7 222041-65-8 222041-66-9 222041-67-0
222041-68-1 222041-69-2 222041-70-5 222041-71-6 222041-72-7
259239-81-1
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(human Fc-.epsilon. receptor CD23 antigen-specific; low-adenosine antisense oligonucleotide agents, compns., kits and treatments for respiratory disorders)

IT 222185-17-3 222185-18-4 222185-19-5 222185-20-8
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(human GM-CSF-specific; low-adenosine antisense oligonucleotide agents, compns., kits and treatments for respiratory disorders)

IT 186556-35-4 222172-44-3 222172-45-4 222172-46-5 222172-48-7
222172-49-8 222172-50-1 222172-51-2 222172-52-3 259239-93-5
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(human **ICAM-1**-specific; low-adenosine antisense oligonucleotide agents, compns., kits and treatments for respiratory disorders)

IT 186556-29-6 222041-74-9 222041-75-0 222041-78-3 222041-81-8
222041-82-9 259239-82-2 259239-83-3 259239-86-6
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(human IgE receptor .alpha.-subunit-specific; low-adenosine antisense oligonucleotide agents, compns., kits and treatments for respiratory disorders)

IT 186556-28-5 222041-61-4 222041-62-5 259239-80-0
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(human IgE receptor .beta.-specific; low-adenosine antisense oligonucleotide agents, compns., kits and treatments for respiratory disorders)

IT 222041-84-1 259239-84-4 259239-85-5
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(human IgE receptor-specific; low-adenosine antisense oligonucleotide agents, compns., kits and treatments for respiratory disorders)

IT 222179-86-4 222179-87-5 222179-89-7 222179-95-5 222179-96-6
222179-97-7 222179-98-8 222180-05-4 222180-11-2 222180-13-4
222180-14-5 222180-15-6 222180-16-7 222180-18-9 222180-22-5
222180-28-1 222180-35-0 222180-43-0 222180-50-9 222180-56-5
222181-21-7 222181-22-8 222181-24-0 222181-26-2 222181-27-3
222181-28-4 222181-29-5 222181-30-8 222181-32-0 222181-33-1
222181-34-2 222181-35-3 222181-36-4 222181-37-5 222181-38-6
222181-39-7 259240-18-1
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(human NF-.kappa.B-specific; low-adenosine antisense oligonucleotide agents, compns., kits and treatments for respiratory disorders)

IT 186556-39-8 222174-79-0
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(human **P selectin**-specific; low-adenosine antisense oligonucleotide agents, compns., kits and treatments for respiratory disorders)

IT 186556-47-8 222042-69-5 222042-70-8 222042-71-9 222042-72-0
222042-73-1 222042-80-0 222042-81-1 222042-82-2 222042-83-3
222042-85-5 222042-86-6 222042-88-8 222042-92-4 259240-03-4
259240-04-5 259240-05-6 259240-06-7 259240-07-8 259240-08-9
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(human RANTES chemokine-specific; low-adenosine antisense oligonucleotide agents, compns., kits and treatments for respiratory disorders)

IT 186556-36-5 222172-84-1 222172-89-6 222172-94-3 222172-95-4
259239-94-6
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(human **VCAM-1**-specific; low-adenosine antisense oligonucleotide agents, compns., kits and treatments for respiratory disorders)

IT 186556-46-7 222042-61-7 222042-62-8
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(human cathepsin G-specific; low-adenosine antisense oligonucleotide agents, compns., kits and treatments for respiratory disorders)

IT 222177-19-7 222177-20-0 222177-21-1 222177-22-2 222177-23-3
222177-24-4 222177-25-5 222177-28-8 222177-34-6 222177-37-9
222177-38-0 222177-40-4 222177-41-5 222177-42-6 222177-43-7
222177-44-8 222177-46-0 222177-47-1 222177-48-2 222177-49-3
222177-50-6
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(human chymase-specific; low-adenosine antisense oligonucleotide agents, compns., kits and treatments for respiratory disorders)

IT 222042-63-9 222042-64-0 222042-65-1 222042-66-2
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(human defensin 1-specific; low-adenosine antisense oligonucleotide agents, compns., kits and treatments for respiratory disorders)

IT 222042-67-3 222042-68-4
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(human defensin 3-specific; low-adenosine antisense oligonucleotide agents, compns., kits and treatments for respiratory disorders)

IT 222177-52-8 222177-53-9 222177-54-0 222177-57-3 222177-63-1
222177-68-6 222177-70-0 222177-73-3 222177-74-4 222177-76-6
222177-77-7 222177-78-8 222177-79-9 222177-84-6 222177-85-7
222177-86-8 222177-92-6 222177-99-3 222178-01-0 222178-02-1
222178-03-2 222178-04-3 222178-07-6 222178-08-7 222178-10-1
222178-11-2 222178-12-3 222178-13-4 222178-14-5 222178-17-8
222178-19-0 222178-21-4 222178-23-6 222178-24-7 222178-25-8
222178-26-9 222178-27-0 222178-29-2 222178-31-6 222178-33-8
222178-34-9 222178-36-1 222178-43-0 222178-51-0 222178-56-5
222178-58-7 222178-60-1 222178-66-7 222178-70-3 222178-72-5
259240-15-8 259240-16-9
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(human **endothelial** nitric oxide synthase-specific; low-adenosine antisense oligonucleotide agents, compns., kits and treatments for respiratory disorders)

IT 222178-54-3 222179-50-2 222179-51-3 222179-52-4 222179-53-5
222179-54-6 222179-81-9 222179-83-1 222179-85-3 222179-88-6
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(human **endothelin** 1-specific; low-adenosine antisense oligonucleotide agents, compns., kits and treatments for respiratory disorders)

IT 222176-39-8 222176-51-4 222176-54-7 222176-62-7 222176-71-8
222176-79-6 222176-84-3 222176-85-4 222176-86-5 222176-87-6
222176-88-7 222176-91-2 222176-92-3 222180-85-0 259240-11-4
259240-12-5
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(human **endothelin** receptor ETA-specific; low-adenosine antisense oligonucleotide agents, compns., kits and treatments for respiratory disorders)

IT 222180-17-8 222180-21-4 222180-57-6 222180-62-3 222180-68-9
222180-76-9
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(human **endothelin** receptor ETB-specific; low-adenosine antisense oligonucleotide agents, compns., kits and treatments for respiratory disorders)

IT 222181-65-9 222181-66-0 222181-67-1 222181-68-2 222181-69-3
222181-70-6 222181-71-7 222181-72-8 222181-73-9 222181-76-2

222181-77-3 222181-78-4 222181-80-8 222181-81-9 222181-82-0
222181-83-1 222181-84-2 222181-85-3 222181-86-4 222181-87-5
222181-88-6 222181-89-7 222181-92-2 222181-93-3 222181-95-5
222181-97-7 222181-98-8 222181-99-9 222182-00-5 222182-01-6
222182-02-7 222182-03-8 222182-04-9 222182-05-0 222182-06-1
222182-07-2 222182-08-3 222182-09-4 222182-10-7 222182-11-8
222182-13-0 222182-15-2 222182-16-3 222182-17-4 222182-19-6
222182-31-2 222182-33-4 222182-34-5 222182-36-7 222182-37-8
222182-39-0 222182-40-3 222182-42-5 222182-45-8 222182-64-1
222182-71-0 222182-80-1 222182-96-9 222182-99-2 222183-08-6
222183-09-7 222183-21-3 222183-22-4 222183-43-9 222183-98-4
223487-18-1 259240-19-2
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(human eosinophil major basic protein-specific; low-adenosine antisense oligonucleotide agents, compns., kits and treatments for respiratory disorders)

IT 186556-34-3 222172-27-2 222172-28-3 222172-34-1 222172-35-2
222172-36-3 222172-37-4 222172-38-5 222172-39-6 222172-40-9
222172-41-0
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(human eosinophil peroxidase-specific; low-adenosine antisense oligonucleotide agents, compns., kits and treatments for respiratory disorders)

IT 222172-03-4 222172-04-5 259239-91-3
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(human eosinophil-derived neurotoxin-specific; low-adenosine antisense oligonucleotide agents, compns., kits and treatments for respiratory disorders)

IT 186556-48-9 222043-23-4 222043-24-5 222043-25-6 222043-26-7
222043-27-8 222043-28-9 222043-29-0 222043-30-3 222043-31-4
222043-32-5 222043-33-6 222043-34-7 222043-35-8 222043-36-9
222043-37-0 222043-38-1 222043-39-2 222043-40-5 222043-41-6
222043-42-7 222043-43-8 222043-44-9
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(human fibronectin-specific; low-adenosine antisense oligonucleotide agents, compns., kits and treatments for respiratory disorders)

IT 186556-30-9 222041-87-4 222041-88-5 222041-89-6 222041-90-9
222041-91-0
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(human histidine decarboxylase-specific; low-adenosine antisense oligonucleotide agents, compns., kits and treatments for respiratory disorders)

IT 222178-76-9 222178-83-8 222178-87-2 222178-97-4 222179-02-4
222179-04-6 222179-08-0 222179-11-5 222179-13-7 222179-18-2
222179-21-7 222179-23-9 222179-25-1 222179-27-3 222179-29-5
222179-31-9 222179-33-1 222179-35-3 222179-37-5 222179-39-7
222179-41-1 222179-42-2 222179-44-4 222179-45-5 222179-47-7
222179-49-9 222179-82-0 259240-17-0
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(human inducible nitric oxide synthase-specific; low-adenosine antisense oligonucleotide agents, compns., kits and treatments for respiratory disorders)

IT 222174-82-5 222174-83-6 222174-84-7 222174-86-9 222174-87-0
222174-88-1 222174-90-5 222174-91-6 222174-92-7 222174-93-8
222174-94-9 222174-95-0 259239-96-8
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(human interleukin 3 receptor-specific; low-adenosine antisense oligonucleotide agents, compns., kits and treatments for respiratory disorders)

IT 186556-40-1 222043-47-2 222043-49-4 222043-52-9 222043-55-2
222043-57-4 222174-80-3 222174-81-4 259240-09-0
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(human interleukin 3-specific; low-adenosine antisense oligonucleotide

agents, compns., kits and treatments for respiratory disorders)

IT 222175-04-4 222175-05-5 222175-06-6 222175-07-7 222175-08-8
222175-09-9 222175-10-2 222175-11-3 222175-12-4 222175-13-5
222175-14-6 222175-15-7 222175-16-8 222175-17-9 222175-18-0
222175-19-1 222175-20-4 222175-21-5 222175-22-6 222175-23-7
222175-24-8 222175-25-9 222175-26-0 222175-27-1 222175-28-2
222175-29-3 222175-30-6 222175-31-7 222175-38-4 222175-42-0
222175-43-1 259239-98-0
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(human interleukin 4 receptor-specific; low-adenosine antisense oligonucleotide agents, compns., kits and treatments for respiratory disorders)

IT 186556-41-2 259239-97-9
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(human interleukin 4-specific; low-adenosine antisense oligonucleotide agents, compns., kits and treatments for respiratory disorders)

IT 222175-62-4 222175-63-5 222175-64-6
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(human interleukin 5 receptor-specific; low-adenosine antisense oligonucleotide agents, compns., kits and treatments for respiratory disorders)

IT 186556-42-3 222175-46-4 222175-47-5 222175-48-6 222175-49-7
222175-50-0 222175-51-1 222175-52-2 259239-99-1
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(human interleukin 5-specific; low-adenosine antisense oligonucleotide agents, compns., kits and treatments for respiratory disorders)

IT 186556-43-4 222533-38-2 222533-39-3 222533-40-6
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(human interleukin 6 receptor-specific; low-adenosine antisense oligonucleotide agents, compns., kits and treatments for respiratory disorders)

IT 222175-65-7 222175-66-8 222175-67-9 222175-68-0 222175-69-1
222175-70-4 222175-72-6 222175-73-7 222175-74-8 222175-75-9
222175-76-0 222175-78-2 222175-79-3 222175-80-6 222175-81-7
222175-82-8 222175-83-9 222175-84-0 222175-85-1 222175-86-2
222175-92-0 222175-93-1 222175-94-2 222175-95-3 222175-96-4
222175-98-6 222176-01-4 222176-07-0 222176-16-1 222176-34-3
222533-36-0 259240-00-1 259240-01-2 260048-15-5
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(human interleukin 6-specific; low-adenosine antisense oligonucleotide agents, compns., kits and treatments for respiratory disorders)

IT 222043-63-2 222043-64-3 222043-65-4 222043-66-5 222043-67-6
222185-13-9 259240-10-3
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(human interleukin 8 receptor .alpha.-specific; low-adenosine antisense oligonucleotide agents, compns., kits and treatments for respiratory disorders)

IT 186556-49-0 222043-60-9 222043-61-0 222043-62-1
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(human interleukin 8-specific; low-adenosine antisense oligonucleotide agents, compns., kits and treatments for respiratory disorders)

IT 186556-51-4 222043-69-8 222043-70-1 222043-71-2 222179-46-6
222179-48-8
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(human leukotriene C4 synthase-specific; low-adenosine antisense oligonucleotide agents, compns., kits and treatments for respiratory disorders)

IT 186556-52-5 222181-40-0 222181-41-1 222181-42-2 222181-46-6
222181-47-7 222181-55-7 222181-62-6
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(human major basic protein-specific; low-adenosine antisense oligonucleotide agents, compns., kits and treatments for respiratory disorders)

IT 186556-45-6 222533-44-0 222533-45-1 222533-46-2 222533-49-5
259240-02-3
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(human medullasin-specific; low-adenosine antisense oligonucleotide agents, compns., kits and treatments for respiratory disorders)

IT 186556-44-5 222533-41-7 222533-42-8
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(human monocyte-derived neutrophil chemotactic factor-specific; low-adenosine antisense oligonucleotide agents, compns., kits and treatments for respiratory disorders)

IT 222043-09-6 222043-10-9 222043-11-0 222043-12-1 222043-13-2
222043-14-3 222043-15-4 222043-16-5 222043-17-6 222043-18-7
222043-19-8 222043-20-1 222043-21-2 222043-22-3
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(human muscarinic acetylcholine receptor HM3-specific; low-adenosine antisense oligonucleotide agents, compns., kits and treatments for respiratory disorders)

IT 222042-95-7 222042-97-9 222042-98-0 222043-02-9 222043-03-0
222043-04-1 222043-05-2 222043-06-3
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(human muscarinic acetylcholine receptor-specific; low-adenosine antisense oligonucleotide agents, compns., kits and treatments for respiratory disorders)

IT 222042-13-9 222042-14-0 222042-15-1 222042-21-9 222042-26-4
222042-36-6 222042-40-2
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(human neutrophil oxidase-specific; low-adenosine antisense oligonucleotide agents, compns., kits and treatments for respiratory disorders)

IT 186556-31-0 222041-98-7 222041-99-8 222042-00-4 222042-01-5
222042-02-6 222042-03-7 222042-05-9 259239-90-2
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(human prostaglandin D synthase-specific; low-adenosine antisense oligonucleotide agents, compns., kits and treatments for respiratory disorders)

IT 222177-06-2 222177-09-5 222177-12-0 222177-14-2 222177-15-3
222177-16-4 259240-13-6 259240-14-7
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(human substance P receptor-specific; low-adenosine antisense oligonucleotide agents, compns., kits and treatments for respiratory disorders)

IT 222176-94-5 222176-95-6 222176-97-8 222177-00-6 222177-02-8
222177-04-0
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(human substance P-specific; low-adenosine antisense oligonucleotide agents, compns., kits and treatments for respiratory disorders)

IT 222041-95-4 259239-89-9
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(human tryptase 1-specific; low-adenosine antisense oligonucleotide agents, compns., kits and treatments for respiratory disorders)

IT 186556-50-3 222179-30-8 222179-36-4 222179-38-6 222179-40-0
222405-89-2 222405-94-9 222405-97-2 222405-99-4 222406-01-1
222406-02-2 222406-03-3 222406-04-4 222406-05-5 222406-07-7
222406-08-8
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(human **tumor** necrosis factor .alpha.-specific; low-adenosine antisense oligonucleotide agents, compns., kits and treatments for respiratory disorders)

IT 222043-68-7 222185-21-9 222185-23-1
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(human **tumor** necrosis factor .alpha.specific; low-adenosine antisense oligonucleotide agents, compns., kits and treatments for respiratory disorders)

IT 186619-39-6 222041-92-1 222041-93-2
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(human .beta.-tryptase-specific; low-adenosine antisense oligonucleotide agents, compns., kits and treatments for respiratory disorders)

IT 58-08-2, biological studies 58-55-9, biological studies 69-89-6
110-85-0, Piperazine, biological studies 479-18-5 519-37-9 652-37-9
890-38-0 2016-63-9 4546-68-3 4546-68-3 5930-94-9 6146-52-7
20535-83-5 41078-02-8 186556-33-2 222171-98-4
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(low-adenosine antisense oligonucleotide agents, compns., kits and treatments for respiratory disorders)

IT 9004-06-2, Elastase
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(neutrophil, **target**; low-adenosine antisense oligonucleotide agents, compns., kits and treatments for respiratory disorders)

IT 84843-69-6, Tryptose
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(receptor, **target**; low-adenosine antisense oligonucleotide agents, compns., kits and treatments for respiratory disorders)

IT 53-43-0 56-81-5, 1,2,3-Propanetriol, biological studies 57-03-4
57-04-5 57-10-3, Hexadecanoic acid, biological studies 62-49-7
63-89-8 96-26-4 107-73-3 563-24-6 987-78-0 9002-92-0 9002-93-1
11029-02-0, Dolichol 17364-18-0 25322-68-3 25322-69-4 26336-38-9
37291-72-8, Polyenoic acid 79331-98-9 95233-18-4 99732-49-7
106392-12-5 108778-82-1, Beractant
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(surfactant for **drug delivery**; low-adenosine antisense oligonucleotide agents, compns., kits and treatments for respiratory disorders)

IT 9001-84-7, Phospholipase A2 9036-21-9 33507-63-0, Substance P
39391-18-9 51982-36-6 56626-18-7, Fucosyltransferase 65154-06-5,
Blood platelet-activating factor 80295-54-1, Complement C5a 80619-02-9
80804-53-1, Complement C3bi 81669-70-7 97501-92-3, Chymase
97501-93-4, Tryptase 103220-14-0, Defensin 106096-93-9 114540-95-3
122653-71-8 125978-95-2 132325-06-5, Defensin NP 1 136661-76-2
141436-78-4 142243-02-5 146239-49-8, Defensin NP 2.alpha.
159606-08-3 165245-96-5
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(**target**; low-adenosine antisense oligonucleotide agents, compns., kits and treatments for respiratory disorders)

IT 131464-24-9 134093-86-0, DNA (human clone 1E11 sialoglycoprotein **VCAM** 1b cDNA) 134711-92-5 134802-79-2 135059-92-6
135639-93-9 136046-25-8 139661-10-2 139804-91-4 139805-49-5
139805-50-8 139805-51-9 139808-09-6 139808-16-5 139808-17-6
139837-57-3 139842-21-0 139844-04-5 139857-92-4 139858-71-2
139868-86-3 139898-85-4 140027-34-5 140029-30-7 140029-31-8
140029-36-3 140029-90-9 140030-54-2 140031-23-8, GenBank K02770
140031-26-1 140031-33-0 140031-38-5 140031-94-3 140032-21-9
140032-22-0 140032-24-2 140032-39-9 140034-18-0 140035-51-4
140036-44-8 140046-39-5 140070-47-9 140070-48-0, GenBank X15265
140079-09-0 140079-10-3 140084-30-6 140086-00-6, GenBank M65001
140092-58-6 140094-50-4 140098-51-7 140109-60-0 140109-61-1
140275-92-9 140277-27-6 140277-88-9 140277-89-0 140277-90-3
140279-21-6, GenBank M11220 140280-37-1 140281-68-1 140281-78-3
140282-11-7 140282-47-9 140282-64-0 140282-70-8 140282-71-9
140284-14-6 140287-35-0 140288-01-3 140304-67-2 140316-98-9
140317-07-3 140325-02-6 140325-03-7 140332-12-3 140332-67-8
140333-25-1 140333-44-4 140337-45-7 140338-87-0, DNA (human gene CMA1 plus flanks) 140343-92-6, DNA (human tachykinin NK1 receptor cDNA

plus 3'-flank) 140344-61-2 140508-22-1 140508-60-7 140513-23-1
140513-71-9 140517-46-0 140580-34-3 140740-31-4 140743-16-4
140744-82-7 140776-11-0 140828-40-6 140983-66-0 141005-40-5
141009-47-4 141162-79-0 141166-97-4 141166-99-6 141167-00-2
141167-01-3 141373-11-7 141705-34-2 141878-70-8 142098-28-0
142693-47-8, DNA (human interleukin 11 gene plus flanks) 142788-98-5
142883-18-9 143003-05-8 143274-62-8 143274-67-3 143342-42-1
143368-90-5 143461-89-6 143461-90-9 143506-54-1 143750-48-5
143899-74-5 145281-49-8 145598-73-8 147401-78-3 147534-25-6
147573-76-0 148283-84-5, DNA (human lung WI-38 cell defensin isoform
HNP-3 gene plus flanks) 148284-15-5 148544-84-7 148955-18-4
148955-19-5 149426-54-0 150219-71-9 150246-86-9 150511-56-1
150859-22-6 150863-54-0, DNA (human interleukin 3 gene 5'-flank)
151151-15-4 151280-39-6 151280-41-0 151576-52-2 151576-86-2
152283-09-5 152472-35-0 152472-36-1 152472-37-2 153056-40-7
153270-02-1 153518-32-2 153638-39-2 153963-49-6, GenBank D28351
153963-66-7, GenBank D28444 154997-81-6 155459-30-6 155610-25-6
156678-85-2 156828-74-9 157111-95-0 157114-64-2 157883-58-4
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160122-04-3 160122-05-4 160122-06-5 160122-07-6 160122-08-7
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166840-83-1 166924-64-7 167713-64-6 167714-05-8 168309-44-2
168385-31-7 168663-08-9 169022-12-2 169278-01-7 169278-02-8
169278-03-9 169278-09-5 169716-15-8 173707-28-3, DNA (human clone 25
eotaxin cDNA) 174057-08-0 174253-63-5 174253-66-8 174253-68-0
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191303-42-1 191303-43-2 191525-64-1 191525-65-2 191525-66-3
RL: PRP (Properties)
(unclaimed nucleotide sequence; low-adenosine antisense oligonucleotide
agents, compns., kits and treatments for respiratory disorders)
IT 192736-48-4 199410-24-7 199413-04-2 200158-82-3 201924-30-3
202944-00-1 204630-23-9 214512-83-1, DNA (human gene DEFB2 plus
flanks) 215917-28-5 218268-18-9 218268-19-0 218268-20-3
219100-45-5 220629-39-0 220629-40-3 220629-41-4 220693-06-1
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222305-45-5 222305-49-9 222305-54-6
RL: PRP (Properties)
(unclaimed nucleotide sequence; low-adenosine antisense oligonucleotide agents, compns., kits and treatments for respiratory disorders)

IT 222305-57-9 222305-62-6 222305-78-4 222306-07-2 222306-12-9
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RL: PRP (Properties)
(unclaimed nucleotide sequence; low-adenosine antisense oligonucleotide agents, compns., kits and treatments for respiratory disorders)

IT 222310-19-2 222310-20-5 222310-21-6 222310-22-7 222310-23-8
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259519-53-4 259519-54-5 259519-55-6 259519-56-7 259519-57-8
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259519-63-6 259519-64-7 259519-65-8 259519-66-9 259519-67-0
259519-68-1 259519-69-2 259519-70-5 259519-71-6 259519-72-7
259519-73-8 259519-74-9 259519-75-0 259519-76-1 259519-77-2
259519-78-3 259519-79-4 259519-80-7 259519-81-8 259519-82-9
259519-83-0 259519-84-1 259519-85-2 259519-86-3 259519-87-4
259519-88-5 259519-89-6 259519-90-9 259540-11-9 259540-12-0
259540-30-2 259540-31-3 259540-43-7 259540-52-8 259540-60-8
259540-64-2 259540-65-3 259540-66-4 259540-67-5 259647-78-4
259647-91-1 259647-92-2 259647-93-3 259647-94-4 259647-95-5
259647-96-6 259647-97-7 259647-98-8 259647-99-9 259648-00-5

RL: PRP (Properties)
(unclaimed nucleotide sequence; low-adenosine antisense oligonucleotide agents, compns., kits and treatments for respiratory disorders)

IT 259648-01-6 259648-02-7 259648-03-8 259648-04-9 259648-05-0
259648-06-1 259648-07-2 259648-08-3 259648-09-4 259668-72-9
259724-09-9 259724-10-2 259724-12-4 259724-13-5 259724-14-6
259724-15-7 259724-16-8 259724-17-9 259724-18-0 259724-19-1
259724-23-7 259724-24-8 259724-25-9 259724-26-0 259724-27-1
259724-28-2 260022-56-8 260022-57-9 260022-58-0 260022-59-1
260022-60-4 260022-61-5 260022-62-6 260022-63-7 260022-64-8
260022-65-9 260022-66-0 260022-67-1 260022-68-2 260022-69-3
260022-70-6 260022-71-7 260022-72-8 260022-73-9 260022-74-0
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260022-85-3 260022-86-4 260022-87-5 260022-88-6 260022-89-7
260022-90-0 260022-91-1 260022-92-2 260022-93-3 260022-94-4
260022-95-5 260022-96-6 260022-97-7 260022-98-8 260043-21-8
260043-43-4 260043-44-5 260043-45-6 260043-46-7 260043-47-8
260043-48-9 260043-49-0 260043-50-3 260043-51-4 260043-52-5
260043-53-6 260043-54-7 260043-55-8 260043-56-9 260043-57-0
260043-58-1 260043-59-2 260043-60-5 260043-61-6 260043-62-7
260043-63-8 260043-64-9 260043-65-0 260043-66-1 260043-67-2
260043-68-3 260043-69-4 260043-70-7 260043-71-8 260043-72-9
260043-73-0 260043-74-1 260043-75-2 260043-76-3 260043-77-4
260043-81-0

RL: PRP (Properties)
(unclaimed nucleotide sequence; low-adenosine antisense oligonucleotide agents, compns., kits and treatments for respiratory disorders)

IT 149200-24-8

RL: PRP (Properties)
(unclaimed nucleotide sequence; w-adenosine antisense oligonucleotide agents, compns., kits and treatments for respiratory disorders)

IT 222301-75-9 260043-07-0 260043-08-1 260043-09-2 260043-10-5
260043-11-6 260043-12-7 260043-13-8 260043-14-9 260043-15-0
260043-16-1 260043-17-2 260043-18-3 260043-20-7 260043-22-9
260043-23-0 260043-24-1 260043-25-2 260043-26-3 260043-27-4
260043-28-5 260043-29-6 260043-30-9 260043-31-0 260043-32-1
260043-33-2 260043-34-3 260043-35-4 260043-36-5 260043-37-6
260043-38-7 260043-39-8 260043-40-1 260043-41-2 260043-42-3
260049-93-2

RL: PRP (Properties)
(unclaimed sequence; low-adenosine antisense oligonucleotide agents, compns., kits and treatments for respiratory disorders)

L56 ANSWER 10 OF 15 HCAPLUS COPYRIGHT 2002 ACS
AN **1999:760629** HCAPLUS
DN **132:97915**
TI Biomimetic transport and rational **drug delivery**
AU Ranney, D. F.
CS Department of Pathology, Department of Radiology, Advanced Radiological Sciences Division, University of Texas Southwestern Medical Center at Dallas, Dallas, TX, USA
SO Biochemical Pharmacology (1999), Volume Date 2000, 59(2), 105-114
CODEN: BCPCA6; ISSN: 0006-2952
PB Elsevier Science Inc.
DT Journal; General Review
LA English
CC 63-0 (Pharmaceuticals)
Section cross-reference(s): 1, **8**
AB A review with 91 refs. Medicine and **pharmaceutics** are encountering crit. needs and opportunities for transvascular **drug delivery** that improves site **targeting** and tissue permeation by mimicking natural tissue addressing and transport

mechanisms. This is driven by the accelerated development of genomic agents requiring **targeted** controlled release. Although rationally designed for in vitro activity, such agents are not highly effective in vivo, due to opsonization and degrdn. by plasma constituents, and failure to transport across the local vascular **endothelium** and tissue matrix. A growing knowledge of the addresses of the body can be applied to engineer "Bio-Logically" staged **delivery** systems with sequential bioaddressins complementary to the discontinuous compartments encountered-termed discontinuum **pharmaceutics**. Effective tissue **targeting** is accomplished by leukocytes, bacteria, and viruses. We are increasingly able to mimic their bioaddressins by genomic means. Approaches described in this commentary include: (a) **endothelial**-directed **adhesion** mediated by oligosaccharides and carbohydrates (**e**.g. dermatan sulfate as a mimic of sulfated CD44) and peptidomimetics interacting with adhesins, **selectins**, integrins, hyaluronans, and locally induced growth factors (**e**.g. vascular **endothelial** growth factor, VEGF) and coagulation factors (**e**.g. factor VIII antigen); (b) improved tissue permeation conferred by hydrophilically "cloaked" **carrier** systems; (c) "uncloaking" by matrix diln. or selective triggering near the **target** cells; and (d) **target binding**-internalization by terminally exposed hydrophobic moieties, cationic polymers, and receptor-**binding** lectins, peptides, or carbohydrates. This commentary also describes intermediate technol. solns. (e.g. "hybrid **drugs**"), and highlights the high-resoln., dynamic magnetic resonance imaging and **radiopharmaceutical** imaging technologies plus the groups and organizations capable of accelerating these important initiatives.

ST review **radiopharmaceutical** transvascular rational **drug delivery**

IT **Radiopharmaceuticals**
(biomimetic transport and rational **drug delivery**)

IT **Blood vessel**
(**endothelium**; biomimetic transport and rational **drug delivery**)

IT **Drug delivery systems**
(transvascular; biomimetic transport and rational **drug delivery**)

RE.CNT 91 THERE ARE 91 CITED REFERENCES AVAILABLE FOR THIS RECORD

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study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(PGSL; **P-selectin** translocation to vascular epithelial lumen by ionizing **radiation**, and therapeutic use)

IT Transcription factors
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(Rb; **P-selectin** translocation to vascular epithelial lumen by ionizing **radiation**, and therapeutic use)

IT Proteins, specific or class
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(**VCAM**; **P-selectin** translocation to vascular epithelial lumen by ionizing **radiation**, and therapeutic use)

IT Proteins, specific or class
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(WT1; **P-selectin** translocation to vascular epithelial lumen by ionizing **radiation**, and therapeutic use)

IT Organelle
(Weibel-Palade body; **P-selectin** translocation to vascular epithelial lumen by ionizing **radiation**, and therapeutic use)

IT Leukocyte
(**adhesion**; **P-selectin** translocation to vascular epithelial lumen by ionizing **radiation**, and therapeutic use)

IT Platelet (blood)
(aggregation; **P-selectin** translocation to vascular epithelial lumen by ionizing **radiation**, and therapeutic use)

IT **Blood vessel, disease**
(arteriovenous malformation; **P-selectin** translocation to vascular epithelial lumen by ionizing **radiation**, and therapeutic use)

IT Disease, animal
(benign, vascular component-assocd.; **P-selectin** translocation to vascular epithelial lumen by ionizing **radiation**, and therapeutic use)

IT Gene, animal
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(c-jun, promoter; **P-selectin** translocation to vascular epithelial lumen by ionizing **radiation**, and therapeutic use)

IT Proteins, specific or class
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(c; **P-selectin** translocation to vascular epithelial lumen by ionizing **radiation**, and therapeutic use)

IT Lung, **neoplasm**
(**carcinoma**, Lewis; **P-selectin** translocation to vascular epithelial lumen by ionizing **radiation**, and therapeutic use)

IT Mammary gland
(**carcinoma**; **P-selectin** translocation to vascular epithelial lumen by ionizing **radiation**, and therapeutic use)

IT Proteins, general, biological studies
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(130,000-mol.-wt.; **P-selectin** translocation to vascular epithelial lumen by ionizing **radiation**, and therapeutic use)

IT Proteins, specific or class
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(150,000-mol.-wt.; **P-selectin** translocation to vascular epithelial lumen by ionizing **radiation**, and therapeutic use)

IT Proteins, specific or class
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(230,000-mol.-wt.; **P-selectin** translocation to vascular epithelial lumen by ionizing **radiation**, and therapeutic use)

IT Ricins
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(A chain, and deglycosylated ricin A chain; **P-selectin** translocation to vascular epithelial lumen by ionizing **radiation**, and therapeutic use)

IT **Selectins**
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(**E-**; **P-selectin** translocation to vascular epithelial lumen by ionizing **radiation**, and therapeutic use)

IT Gene, animal
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(Egr-1, promoter; **P-selectin** translocation to vascular epithelial lumen by ionizing **radiation**, and therapeutic use)

IT **Cell adhesion molecules**
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(**ICAM-1** (**intercellular adhesion mol. 1**); **P-selectin** translocation to vascular epithelial lumen by ionizing **radiation**, and therapeutic use)

IT Blood-group substances
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(Lea, sialyl; **P-selectin** translocation to vascular epithelial lumen by ionizing **radiation**, and therapeutic use)

IT Blood-group substances
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(Lex, sialyl; **P-selectin** translocation to vascular epithelial lumen by ionizing **radiation**, and therapeutic use)

IT **Selectins**
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(**P-**; **P-selectin** translocation to vascular epithelial lumen by ionizing **radiation**, and therapeutic use)

IT Cell

(**P-selectin binding** component; **P**
-selectin translocation to vascular epithelial lumen by
ionizing **radiation**, and therapeutic use)

IT **Antibodies**
Glycolipids
Glycoproteins, specific or class
Oligosaccharides, biological studies
Polysaccharides, biological studies
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(**P-selectin binding** component; **P**
-selectin translocation to vascular epithelial lumen by
ionizing **radiation**, and therapeutic use)

IT Alkylating agents, biological
Anti-inflammatory agents
Antibiotics
Antitumor agents
Blood vessel
Cardiovascular agents
Chemotherapy
Cytotoxic agents
Drug delivery systems
Drug targeting
Eosinophil
Fluorescent substances
Gamma ray
Genetic vectors
Ionizing **radiation**
Oxidizing agents
Paramagnetic materials
Polymorphonuclear leukocyte
Radiation
Radioprotectants
Radiotherapy
Retroviral vectors
Signal transduction, biological
T cell (lymphocyte)
Thrombolytics
X-ray
(**P-selectin** translocation to vascular epithelial
lumen by ionizing **radiation**, and therapeutic use)

IT Anthracyclines
Interleukin 12
Lipid A
Steroids, biological studies
Toxins
Tumor necrosis factors
p53 (protein)
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(**P-selectin** translocation to vascular epithelial
lumen by ionizing **radiation**, and therapeutic use)

IT Interleukin 1
Radionuclides, biological studies
Tumor necrosis factors
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(**P-selectin** translocation to vascular epithelial
lumen by ionizing **radiation**, and therapeutic use)

IT Oligosaccharides, biological studies
RL: BAC (Biological activity or effector, except adverse); BSU (Biological

(**carrier**; **P-selectin** translocation to vascular epithelial lumen by ionizing **radiation**, and therapeutic use)

IT Ligands
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(cell, **P-selectin binding** component; **P-selectin** translocation to vascular epithelial lumen by ionizing **radiation**, and therapeutic use)

IT Intestine, **neoplasm**
(colon, **carcinoma**; **P-selectin** translocation to vascular epithelial lumen by ionizing **radiation**, and therapeutic use)

IT Eye, disease
(diabetic retinopathy; **P-selectin** translocation to vascular epithelial lumen by ionizing **radiation**, and therapeutic use)

IT Toxins
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(diphtheria; **P-selectin** translocation to vascular epithelial lumen by ionizing **radiation**, and therapeutic use)

IT **Blood vessel**
(**endothelium**; **P-selectin** translocation to vascular epithelial lumen by ionizing **radiation**, and therapeutic use)

IT Pseudomonas
(exotoxin; **P-selectin** translocation to vascular epithelial lumen by ionizing **radiation**, and therapeutic use)

IT Toxins
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(exotoxins, Pseudomonas; **P-selectin** translocation to vascular epithelial lumen by ionizing **radiation**, and therapeutic use)

IT **Radiation**
(exposure, detn.; **P-selectin** translocation to vascular epithelial lumen by ionizing **radiation**, and therapeutic use)

IT Neuroglia
(glioma; **P-selectin** translocation to vascular epithelial lumen by ionizing **radiation**, and therapeutic use)

IT Temperature effects, biological
(heat; **P-selectin** translocation to vascular epithelial lumen by ionizing **radiation**, and therapeutic use)

IT Lung, disease
(inflammation; **P-selectin** translocation to vascular epithelial lumen by ionizing **radiation**, and therapeutic use)

IT Receptors
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(inflammatory cell; **P-selectin** translocation to vascular epithelial lumen by ionizing **radiation**, and therapeutic use)

IT **Drug delivery systems**
(injections; **P-selectin** translocation to vascular epithelial lumen by ionizing **radiation**, and therapeutic use)

IT **Drug delivery systems**
(instillation; **P-selectin** translocation to vascular epithelial lumen by ionizing **radiation**, and therapeutic use)

IT NMR (nuclear magnetic resonance)
(isotope, marker; **P-selectin** translocation to vascular epithelial lumen by ionizing **radiation**, and therapeutic use)
IT Cell **adhesion**
(leukocyte; **P-selectin** translocation to vascular epithelial lumen by ionizing **radiation**, and therapeutic use)
IT **Drug delivery systems**
(**liposomes**; **P-selectin** translocation to vascular epithelial lumen by ionizing **radiation**, and therapeutic use)
IT Gene, animal
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(los, promoter; **P-selectin** translocation to vascular epithelial lumen by ionizing **radiation**, and therapeutic use)
IT Meninges
Meninges
Meninges
(meningioma, inhibitors; **P-selectin** translocation to vascular epithelial lumen by ionizing **radiation**, and therapeutic use)
IT **Antitumor** agents
Antitumor agents
Antitumor agents
(meningioma; **P-selectin** translocation to vascular epithelial lumen by ionizing **radiation**, and therapeutic use)
IT **Antibodies**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(monoclonal, **P-selectin binding** component; **P-selectin** translocation to vascular epithelial lumen by ionizing **radiation**, and therapeutic use)
IT Lymphocyte
(natural killer cell; **P-selectin** translocation to vascular epithelial lumen by ionizing **radiation**, and therapeutic use)
IT **Drug delivery systems**
(oral; **P-selectin** translocation to vascular epithelial lumen by ionizing **radiation**, and therapeutic use)
IT Proteins, specific or class
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(p16; **P-selectin** translocation to vascular epithelial lumen by ionizing **radiation**, and therapeutic use)
IT **Drug delivery systems**
(parenterals; **P-selectin** translocation to vascular epithelial lumen by ionizing **radiation**, and therapeutic use)
IT Oligosaccharides, biological studies
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(pentasaccharides, sialyl Lewis; **P-selectin** translocation to vascular epithelial lumen by ionizing **radiation**, and therapeutic use)
IT Cell aggregation
(platelet; **P-selectin** translocation to vascular epithelial lumen by ionizing **radiation**, and therapeutic use)
IT **Proliferation** inhibition
(**proliferation** inhibitors; **P-selectin**

translocation to vascular epithelial lumen by ionizing **radiation**, and therapeutic use)

IT Leukocyte
(receptor; **P-selectin** translocation to vascular epithelial lumen by ionizing **radiation**, and therapeutic use)

IT **Artery, disease**
(restenosis; **P-selectin** translocation to vascular epithelial lumen by ionizing **radiation**, and therapeutic use)

IT **Selectins**
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(**selectin-binding** agents; **P-selectin** translocation to vascular epithelial lumen by ionizing **radiation**, and therapeutic use)

IT **Antitumor** agents
(solid **tumor**; **P-selectin** translocation to vascular epithelial lumen by ionizing **radiation**, and therapeutic use)

IT Oligosaccharides, biological studies
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(sulfated, sulfated Le penta- and tetrasaccharides; **P-selectin** translocation to vascular epithelial lumen by ionizing **radiation**, and therapeutic use)

IT Oligosaccharides, biological studies
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(tetrasaccharides, sialyl Lewis; **P-selectin** translocation to vascular epithelial lumen by ionizing **radiation**, and therapeutic use)

IT Gene
RL: BPR (Biological process); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(therapeutic-encoding; **P-selectin** translocation to vascular epithelial lumen by ionizing **radiation**, and therapeutic use)

IT **Drug delivery systems**
(topical; **P-selectin** translocation to vascular epithelial lumen by ionizing **radiation**, and therapeutic use)

IT Bacteria (Eubacteria)
Fungi
Plant (Embryophyta)
(toxin; **P-selectin** translocation to vascular epithelial lumen by ionizing **radiation**, and therapeutic use)

IT Lymphocyte
(**tumor**-infiltrating; **P-selectin** translocation to vascular epithelial lumen by ionizing **radiation**, and therapeutic use)

IT Adeno-associated virus
Adenoviridae
Human herpesvirus 1
Human papillomavirus
Vaccinia virus
(vector; **P-selectin** translocation to vascular epithelial lumen by ionizing **radiation**, and therapeutic use)

IT Alkaloids, biological studies
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(vinca; **P-selectin** translocation to vascular epithelial lumen by ionizing **radiation**, and therapeutic use)

IT Interferons

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(.alpha.; **P-selectin** translocation to vascular epithelial lumen by ionizing **radiation**, and therapeutic use)

IT Interferons
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(.beta.; **P-selectin** translocation to vascular epithelial lumen by ionizing **radiation**, and therapeutic use)

IT Interferons
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(.gamma.; **P-selectin** translocation to vascular epithelial lumen by ionizing **radiation**, and therapeutic use)

IT 7722-84-1, Hydrogen peroxide (H2O2), biological studies 7782-44-7, Oxygen, biological studies
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(**P-selectin** translocation to vascular epithelial lumen by ionizing **radiation**, and therapeutic use)

IT 67-99-2, Aspergillin 131-49-7, Renografin 1260-17-9, Carminic acid 1405-86-3, Glycyrrhizin 1406-72-0, Restrictocin 1407-48-3, .alpha.-Sarcin 4375-07-9, Epipodophyllotoxin 7429-91-6, Dysprosium, biological studies 7439-89-6, Iron, biological studies 7439-96-5, Manganese, biological studies 7440-00-8, Neodymium, biological studies 7440-02-0, Nickel, biological studies 7440-19-9, Samarium, biological studies 7440-27-9, Terbium, biological studies 7440-47-3, Chromium, biological studies 7440-48-4, Cobalt, biological studies 7440-50-8, Copper, biological studies 7440-52-0, Erbium, biological studies 7440-54-2, Gadolinium, biological studies 7440-60-0, Holmium, biological studies 7440-62-2, Vanadium, biological studies 7440-64-4, Ytterbium, biological studies 7481-89-2, Dideoxycytidine 9001-99-4, Ribonuclease 9002-01-1, Streptokinase 9002-06-6, Thymidine kinase 9014-02-2, Neocarzinostatin 9025-05-2, Cytosine deaminase 10043-49-9, Gold-198, biological studies 10043-66-0, Iodine-131, biological studies 10045-97-3, Cesium-137, biological studies 10098-91-6, Yttrium-90, biological studies 10198-40-0, Cobalt-60, biological studies 13982-63-3, Radium-226, biological studies 14119-09-6, Gallium-67, biological studies 14158-31-7, Iodine-125, biological studies 14378-26-8, Rhenium-188, biological studies 14596-37-3, Phosphorus-32, biological studies 14694-69-0, Iridium-192, biological studies 14998-63-1, Rhenium-186, biological studies 15715-08-9, Iodine-123, biological studies 15750-15-9, Indium-111, biological studies 15755-39-2, Astatine-211, biological studies 15757-86-5, Copper-67, biological studies 25316-40-9, Adriamycin 75037-46-6, Gelonin 92448-22-1 98603-84-0 100787-31-3, Polylactosamine 168678-84-0, Cylexin
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(**P-selectin** translocation to vascular epithelial lumen by ionizing **radiation**, and therapeutic use)

IT 109319-16-6 141436-78-4, Protein kinase C
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(**P-selectin** translocation to vascular epithelial lumen by ionizing **radiation**, and therapeutic use)

IT 2462-63-7, DOPE 104162-48-3, DOTMA 153985-22-9, DORIE
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(**P-selectin** translocation to vascular epithelial

lumen by ionizing **radiation**, and therapeutic use)

IT 14133-76-7, Technetium-99, biological studies
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(**metastable; P-selectin** translocation to vascular epithelial lumen by ionizing **radiation**, and therapeutic use)

RE.CNT 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD

RE

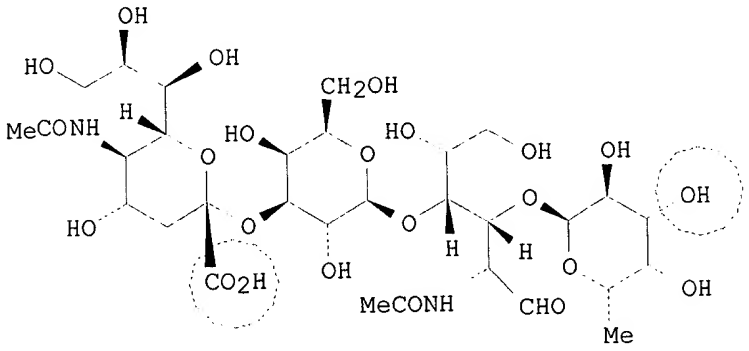
(1) ARCH Development Corporation; WO 9625947 A 1996 HCAPLUS
(2) Barker, J; CIBA Foundation Symposium 1995, V189, P91 HCAPLUS
(3) Berg, E; Blood 1995, V85(1), P31 HCAPLUS
(4) Dulkanchainun, T; Annals of Surgery 1998, V227(6), P832 MEDLINE
(5) McEver, R; Journal of Cellular Biochemistry 1991, V45(2), P156 HCAPLUS
(6) Sluiter; J Cardiovasc Pharmacol 1993, V22(4), PS37

L56 ANSWER 12 OF 15 HCAPLUS COPYRIGHT 2002 ACS
AN **1997:475136** HCAPLUS
DN **127:130998**
TI Methods of treating inflammation using selection-**binding** compounds
IN Brandley, Brian K.; Tiemeyer, Michael; Swiedler, Stuart J.; Moreland, Margaret; Schweingruber, Hans; Rao, Narasinga
PA Glycomed Incorporated, USA
SO U.S., 20 pp., Cont.-in-part of U.S. 5,211,937.
CODEN: USXXAM
DT Patent
LA English
IC ICM A01N043-04
NCL 514061000
CC 1-7 (Pharmacology)
Section cross-reference(s): 63

FAN.CNT 4

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 5648344	A	19970715	US 1992-922328	19920730
	US 5211936	A	19930518	US 1990-559836	19900730
	US 5143712	A	19920901	US 1991-637868	19910107
	US 5211937	A	19930518	US 1991-683458	19910411
	CA 2100600	AA	19940131	CA 1993-2100600	19930715
	AU 9342111	A1	19940203	AU 1993-42111	19930721
	AU 665431	B2	19960104		
	NO 9302665	A	19940131	NO 1993-2665	19930723
	EP 589556	A2	19940330	EP 1993-306071	19930730
	EP 589556	A3	19951227		
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE				
	JP 06206892	A2	19940726	JP 1993-190627	19930730
PRAI	US 1990-559836		19900730		
	US 1990-613113		19901115		
	US 1991-637868		19910107		
	US 1991-683458		19910411		
	US 1990-559856		19900730		
	US 1992-922328		19920730		

OS MARPAT 127:130998
GI



I

AB Ligands that **bind** to human **selectin** receptors are disclosed. The ligands are formulated with excipient **carriers** to form compns. which are administered to treat conditions such as inflammation. The ligands have the structural formula I or mols. which have hydrogen bond donor groups equiv. to the circled groups with respect to their ability to form hydrogen bonds with a **selectin** under physiol. conditions. The **selectin** is e.g. ELAM-1. **Radiolabeled** COS cells expressing cell-surface ELAM-1 were used as probes to screen human leukocyte-derived glycolipids.

ST **selectin** ligand glycolipid inflammation treatment; ELAM1 ligand glycolipid inflammation treatment

IT **Selectins**
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(**E**-; selection-**binding** compds. for treatment of inflammation)

IT Neutrophil
(glycolipids; selection-**binding** compds. for treatment of inflammation)

IT **Drug delivery systems**
(injections, i.v.; selection-**binding** compds. for treatment of inflammation)

IT **Drug delivery systems**
(injections; selection-**binding** compds. for treatment of inflammation)

IT Anti-inflammatory agents
(selection-**binding** compds. for treatment of inflammation)

IT Carbohydrates, biological studies
Glycolipids
RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(selection-**binding** compds. for treatment of inflammation)

IT **Selectins**
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(selection-**binding** compds. for treatment of inflammation)

IT 7440-70-2, Calcium, biological studies
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(calcium requirement in glycolipid **binding** to COS cells expressing cell-surface ELAM-1)

IT 92448-22-1 98603-84-0 193140-26-0
RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); THU (Therapeutic use);

BIOL (Biological study); PROC (Process); USES (Uses)
(selection-**binding** compds. for treatment of inflammation)

L56 ANSWER 13 OF 15 HCAPLUS COPYRIGHT 2002 ACS
AN **1997:151854** HCAPLUS
DN **126:246178**
TI **Tumor** vascular **endothelium**: barrier or **target** in **tumor** directed **drug delivery** and immunotherapy
AU Molema, Grietje; de Leij, Lou F. M. H.; Meijer, Dirk K. F.
CS Dep. Clinical Immunology, Univ. Hospital Groningen, Groningen, 9713 GZ, Neth.
SO Pharmaceutical Research (1997), 14(1), 2-10
CODEN: PHREEB; ISSN: 0724-8741
PB Plenum
DT Journal; General Review
LA English
CC 1-0 (Pharmacology)
Section cross-reference(s): 63
AB A review, with 68 refs. The therapy of solid **tumors** with conventional **chemotherapeutics, drug delivery** prepns. and immunomodulatory agents directed against the **tumor** cells is corrupted by a major barrier presented by the **tumor** vasculature. Permeability of the **tumor** blood vessels for transport of small mols. and macromol. **drug-carrier conjugates** is only sufficient in the blood vessels at the **tumor**-host interface. Down-regulation of the expression of **adhesion** mols., required for the facilitation of immune cell recruitment, by the **tumor** vascular **endothelium** results in an escape of the **tumor** from host defense. New therapeutic approaches for the treatment of solid **tumors** are aimed at the **tumor** vasculature, either at the **endothelial** cells themselves or at basement membrane or **tumor** stroma components. Angiogenesis can be directly blocked with angiogenesis inhibitors, while angiogenesis related factors can serve as **tumor** vasculature specific epitopes for **drug delivery** strategies. Some glycoproteins expressed by **tumor endothelial** cells or present in the basement membrane and **tumor** stroma are also potential **tumor** selective **targets**. Therapeutic modalities that are suitable for site specific **delivery** are agents that increase **tumor** accumulation of (**targeted**) chemo/**radiotherapeutics** through increasing **tumor** vascular permeability. The observation that for **tumor** growth the blood supply is a limiting factor, led to the development of strategies to inhibit angiogenesis or block the **tumor** blood flow. Manipulation of the expression of **endothelial cell adhesion mols.** by selectively **delivering** modulatory agents at or in the **tumor** vascular **endothelial** cells may induce (bispecific **antibody** mediated) host defense activity directed against the **tumor** cells.
ST review **antitumor targeting tumor** vascular **endothelium**; immunotherapy **tumor** vascular **endothelium** review
IT **Blood vessel**
(**endothelium, tumor; tumor** vascular **endothelium** as **target** in **tumor** directed **drug delivery** and immunotherapy)
IT **Antitumor** agents
Drug delivery systems
Immunotherapy
(**tumor** vascular **endothelium** as **target** in **tumor** directed **drug delivery** and

immunotherapy)

L56 ANSWER 14 OF 15 HCAPLUS COPYRIGHT 2002 ACS
AN **1997:6022** HCAPLUS
DN **126:37037**
TI Myeloglycans for treatment of **selectin**-mediated disorders
IN Handa, Kazuko; Stroud, Mark R.; Levery, Steven B.; Toyokuni, Tatsushi; Hakomori, Sen-itiroh; Song, Yu
PA The Biomembrane Institute, USA; Handa, Kazuko; Stroud, Mark R.; Levery, Steven B.; Toyokuni, Tatsushi; Hakomori, Sen-Itiroh; Song, Yu
SO PCT Int. Appl., 70 pp.
CODEN: PIXXD2
DT Patent
LA English
IC ICM A61K031-725
ICS C08B037-00
CC 63-3 (Pharmaceuticals)
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 9634609	A1	19961107	WO 1996-US6120	19960503

W: CA, JP, US
RW: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE

PRAI US 1994-353328 19941205
US 1995-435664 19950505

AB Myeloglycan oligosaccharides [NeuAc-.alpha.(2.fwdarw.3)-Gal-.beta.(1.fwdarw.4)-GlcNAc(R1)-.beta.(1.fwdarw.3)-[Gal-.beta.(1.fwdarw.4)-GlcNAc(R2)-.beta.(1.fwdarw.3)]3-20; R1, R2 = H, .alpha.(1.fwdarw.3)-Fuc] which **bind E-selectin** are extd. from immune system cells (**e**.g. lymphocytes) for use as inhibitors of cell aggregation and inflammation. Systematic chem. anal. of glycosphingolipid fractions from normal human neutrophils and HL60 cells failed to detect glycosphingolipids which are **binding targets** of **selectin**. Long-chain, unbranched polylactosamine glycosphingolipids contg. these myeloglycan oligosaccharides, rather than sialyl-Lex, are the physiol. **E-selectin-binding** moieties on immune system cells. The myeloglycan may be attached via the terminal GlcNAc residue to a bifunctional linker and/or an OH group of a **carrier**, and may be incorporated into microspheres or **liposomes**. Thus, **binding** of **radiolabeled** leukocytes at a **selectin**-expressing injury site in mice was reduced by pretreatment with myeloglycan.

ST inflammation inhibitor myeloglycan oligosaccharide; lymphocyte lactosamine oligosaccharide **binding selectin**

IT **Selectins**
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(**E**-; myeloglycans for treatment of **selectin**-mediated disorders)

IT Leukocyte
(**E-selectin binding** of, in injury; myeloglycans for treatment of **selectin**-mediated disorders)

IT Glycosphingolipids
Oligosaccharides, biological studies
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(lactosamine-contg.; myeloglycans for treatment of **selectin**-mediated disorders)

IT **Drug delivery systems**
(**liposomes**; myeloglycans for treatment of **selectin**-mediated disorders)

IT **Drug delivery systems**

(microspheres; myeloglycans for treatment of **selectin**-mediated disorders)

IT New natural products
(myeloglycans (oligosaccharides))

IT Anti-inflammatory agents
Cell aggregation
(myeloglycans for treatment of **selectin**-mediated disorders)

IT Lymphocyte
(myeloglycans of; myeloglycans for treatment of **selectin**-mediated disorders)

IT Molecular structure, natural product
(of myeloglycans (oligosaccharides))

IT **Carriers**
Coupling agents
(oligosaccharide **conjugates**; myeloglycans for treatment of **selectin**-mediated disorders)

IT 56-45-1D, L-Serine, oligosaccharide **conjugates**, biological studies 72-19-5D, Threonine, oligosaccharide **conjugates**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(of **carrier**; myeloglycans for treatment of **selectin**-mediated disorders)

IT 184642-15-7 184642-16-8 184642-17-9 184642-18-0 184642-19-1
184642-20-4 184642-21-5 184642-22-6 184642-24-8 184642-27-1
184642-29-3 184642-31-7 184642-33-9 184642-35-1
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(oligosaccharide-terminating; myeloglycans for treatment of **selectin**-mediated disorders)

L56 ANSWER 15 OF 15 HCAPLUS COPYRIGHT 2002 ACS
AN **1992:228245** HCAPLUS
DN **116:228245**
TI **Selectin-binding** intercellular **adhesion** mediators for **pharmaceuticals**
IN Paulson, James C.; Perez, Mary S.; Gaeta, Federico C. A.; Ratcliffe, Robert Murray
PA Cytel Corp., USA
SO PCT Int. Appl., 108 pp.
CODEN: PIXXD2
DT Patent
LA English
IC ICM A61K031-70
ICS A61K037-02; A61K039-00; A61K037-20
CC 1-7 (Pharmacology)
Section cross-reference(s): 15, 63
FAN.CNT 3

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9119502	A1	19911226	WO 1991-US4284	19910614
	W: AT, AU, BB, BG, BR, CA, CH, DE, DK, ES, FI, GB, HU, JP, KP, KR, LK, LU, MC, MG, MW, NL, NO, PL, RO, SD, SE, SU				
	RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, DE, DK, ES, FR, GA, GB, GN, GR, IT, LU, ML, MR, NL, SE, SN, TD, TG				
	WO 9119501	A1	19911226	WO 1991-US3592	19910522
	W: AT, AU, BB, BG, BR, CA, CH, DE, DK, ES, FI, GB, HU, JP, KP, KR, LK, LU, MC, MG, MW, NL, NO, PL, RO, SD, SE, SU				
	RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, DE, DK, ES, FR, GA, GB, GR, IT, LU, ML, MR, NL, SE, SN, TD, TG				
	AU 9181029	A1	19920107	AU 1991-81029	19910614
	AU 660931	B2	19950713		

	ZA 9104557	A	19920325	ZA 1991-4557	19910614
	EP 533834	A1	19930331	EP 1991-912402	19910614
	R: AT, BE, CH, DE, DK, ES, FR, GB, IT, LI, LU, NL, SE				
	BR 9106556	A	19930720	BR 1991-6556	19910614
	RU 2123338	C1	19981220	RU 1992-16522	19910614
	NO 9204830	A	19930208	NO 1992-4830	19921214
PRAI	US 1990-538853	A	19900615		
	US 1990-619319	A	19901128		
	US 1990-632390	A	19901221		
	WO 1991-US3592	A	19910522		
	WO 1991-US4284	A	19910614		

OS MARPAT 116:228245

AB Compns. and methods for reducing or controlling inflammation and for treating inflammatory disease processes and other pathol. conditions mediated by **selectin**-mediated intercellular **adhesion** are disclosed. The **pharmaceutical** compns. comprise a **carrier** and compds. which selectively **bind** **selectin**, e.g. biomols. contg. R1Gal.beta.1,4(Fuc.alpha.1,3)GlcNAcR2a [R1 = oligosaccharide, R3R4C(CO2H); R3, R4 = H, C1-8 alkyl, hydroxyl C1-8 alkyl, aryl C1-8 alkyl, alkoxy C1-8 alkyl; R2 = .beta.1,3Gal, .perp.,2Man, .alpha.1,6GalNAc; a = 0,1]. Rats were protected from endotoxic shock by treatment with monoclonal **antibody** P6E2 to human ELAM-1 protein.

ST **selectin** intercellular **adhesion** inhibition; inflammation inhibitor **selectin binding** oligosaccharide; endotoxic shock monoclonal **antibody** ELAM1; protein ELAM1 **antibody** endotoxic shock; **pharmaceutical** **selectin binding** oligosaccharide

IT **Endothelium**
(cell of, leukocyte or monocyte **adhesion** to, inhibition of, with **selectin-binding** compds.)

IT Monocyte
Neutrophil
(**endothelial** cell **adhesion** to, inhibition of, with **selectin-binding** compds.)

IT Lipopolysaccharides
RL: BIOL (Biological study)
(endotoxic shock from, protection from, in rat, with monoclonal **antibody** P6E2 to human ELAM-1 protein)

IT Polysaccharides, compounds
RL: BIOL (Biological study)
(fucosylated type Ia, **selectin-binding**, of Group B Streptococcus, **pharmaceutical** contg.)

IT Escherichia coli
(lipopolysaccharide of, endotoxic shock from, protection from, in rat, with monoclonal **antibody** P6E2 to human ELAM-1 protein)

IT Analysis
(of compds. inhibiting **selectin**-mediated cellular **adhesion**, **selectin binding** inhibition in)

IT **Pharmaceutical dosage forms**
(of **selectin-binding** compds.)

IT Blood platelet
(**selectin** on, oligosaccharide **binding**, for **pharmaceuticals**)

IT Inflammation inhibitors
(**selectin-binding** compds.)

IT Leukocyte
(**selectin-binding** oligosaccharide expressed by, Igs to, for **pharmaceuticals**)

IT Ligands
RL: BIOL (Biological study)
(**selectin-binding** oligosaccharide, Igs to, for **pharmaceuticals**)

IT Gangliosides
Lipids, biological studies
Oligosaccharides
Polysaccharides, biological studies
Proteins, specific or class
Sphingolipids
RL: BIOL (Biological study)
(**selectin-binding**, for **pharmaceuticals**)

IT Immunoglobulins
RL: BIOL (Biological study)
(to **selectin-binding** oligosaccharide, for **pharmaceuticals**)

IT Respiratory distress syndrome
(treatment of acute, with compd. **binding** selection)

IT Sepsis and Septicemia
(treatment of wound-assocd., with compd. **binding** selection)

IT Polysaccharides, compounds
RL: BIOL (Biological study)
(type II, **selectin-binding**, of Group B Streptococcus, **pharmaceutical** contg.)

IT Polysaccharides, compounds
RL: BIOL (Biological study)
(type III, **selectin-binding**, of Group B Streptococcus, **pharmaceutical** contg.)

IT Glycopeptides
RL: BIOL (Biological study)
(with **selectin-binding** oligosaccharide, for **pharmaceuticals**)

IT Golgi apparatus
(.alpha.1,3-fucosyltransferase isolation from)

IT Glycoproteins, specific or class
RL: BIOL (Biological study)
(ELAM-1 (**endothelial** leukocyte **adhesion** mol. 1), oligosaccharide **binding**, for **pharmaceuticals**)

IT Glycoproteins, specific or class
RL: BIOL (Biological study)
(GMP-140 (.alpha.-**granule** membrane protein, 140,000-mol.-wt.), oligosaccharide **binding**, for **pharmaceuticals**)

IT Animal cell line
(HL-60, intercellular **adhesion** between activated HUVEC cells and, inhibition of, with monoclonal **antibodies** to sialylated Lex)

IT Animal cell line
(HUVEC, activated, intercellular **adhesion** between HL-60 cells and, inhibiton of, with monoclonal **antibodies** to sialylated Lex)

IT **Adhesion**
(bio-, **selectin**-mediated, inhibition of, with compd. **binding selectin**)

IT Molecules
(biochem., **selectin-binding**, for **pharmaceuticals**)

IT Carbohydrates and Sugars, compounds
RL: BIOL (Biological study)
(**conjugates**, inhibiting **selectin**-mediated cellular **adhesion**, detn. of, **selectin binding** inhibition in)

IT Amino acids, compounds
Glycolipids
Glycoproteins, specific or class
RL: BIOL (Biological study)
(**conjugates**, * **-binding oligosaccharide**,

for pharmaceuticals GlycolipidslROLES **AS**)

IT Newborn
(disorder, respiratory distress syndrome, treatment of acute, with compd. **binding** selection)

IT **Blood vessel, composition**
(**endothelium**, cell of, **selectin** receptor on, oligosaccharide **binding**, for **pharmaceuticals**)

IT Shock
(endotoxin, protection from, in rat, with monoclonal **antibody** P6E2 to human ELAM-1 protein)

IT Streptococcus
(group B, **selectin-binding** polysaccharides of, **pharmaceutical** contg.)

IT **Pharmaceutical dosage forms**
(**liposomes, selectin-binding** compds. on)

IT **Neoplasm** inhibitors
(**metastasis, selectin-binding** compds. as)

IT **Antibodies**
RL: BIOL (Biological study)
(monoclonal, to sialylated Lex, intercellular **adhesion** between activated HUVEC cells and HL-60 cells inhibition with)

IT Peptides, biological studies
RL: BIOL (Biological study)
(oligo-, **selectin-binding**, for **pharmaceuticals**)

IT **Glycoproteins, specific or class**
RL: BIOL (Biological study)
(**selectins**, compds. **binding**, for **pharmaceuticals**)

IT Shock
(septic, treatment of, with compd. **binding selectin**
)

IT 52720-51-1, Endo-.beta.-galactosidase
RL: BIOL (Biological study)
(HL-60 cells treatment with, activated blood platelets response to)

IT 56-41-7, Alanine, biological studies 60-18-4, Tyrosine, biological studies 60-18-4D, Tyrosine, **radioiodinated**
RL: BIOL (Biological study)
(glycooligopeptide contg. **selectin-binding** oligosaccharide and, for **pharmaceuticals**)

IT 140936-84-1
RL: BIOL (Biological study)
(homopolymers of **selectin-binding** polysaccharide contg., **pharmaceutical** contg.)

IT 90327-80-3 92480-43-8
RL: BIOL (Biological study)
(**liposomes** contg., intercellular **adhesion** between activated HUVEC cells and HL-60 cells inhibition with)

IT 73201-40-8, Lex
RL: BIOL (Biological study)
(monoclonal **antibodies** to, intercellular **adhesion** between activated HUVEC cells and HL-60 cells inhibition with)

IT 140938-81-4
RL: BIOL (Biological study)
(neutrophils **binding** to activated blood platelets inhibition with)

IT 141175-62-4 141175-63-5 141175-64-6
RL: BIOL (Biological study)
(neutrophils **binding** to activated blood platelets inhibition with **liposomes** contg.)

IT 96119-72-1 141175-61-3
RL: BIOL (Biological study)
(neutrophils **binding** to activated blood platelets response to

liposomes contg.)
IT 39279-34-0
RL: BIOL (Biological study)
(oligosaccharide fucosylation with, in **selectin-binding** compd. prepn.)
IT 53-86-1, Indomethacin 22204-53-1, Naproxen 24280-93-1, Mycophenolic acid 59865-13-3, Cyclosporin A 104987-11-3, FK-506
RL: BIOL (Biological study)
(**selectin-binding** oligosaccharide on **liposome** encapsulating)
IT 56-87-1D, L-Lysine, oligosaccharide **conjugates** 70-26-8D, Ornithine, oligosaccharide **conjugates** 70-47-3D, Asparagine, oligosaccharide **conjugates** 110-85-0D, Piperazine, oligosaccharide **conjugates** 305-62-4D, oligosaccharide **conjugates** 498-56-6D, Homolysine, oligosaccharide **conjugates** 505-66-8D, Homopiperazine, oligosaccharide **conjugates** 13184-13-9D, oligosaccharide **conjugates** 71292-18-7D, oligosaccharide **conjugates**
RL: BIOL (Biological study)
(**selectin-binding**, for **pharmaceuticals**)
IT 98603-84-0 140913-62-8 140913-63-9 140913-64-0 140913-65-1 140913-66-2 140913-67-3 140913-68-4 140913-69-5 140913-70-8 141024-33-1 141042-38-8
RL: BIOL (Biological study)
(**selectin-binding, pharmaceutical liposome** compn. contg.)

=> fil wpix
FILE 'WPIX' ENTERED AT 13:11:10 ON 15 AUG 2002
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FILE LAST UPDATED: 12 AUG 2002 <20020812/UP>
MOST RECENT DERWENT UPDATE 200251 <200251/DW>
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=> d all abeq tech abex tot

L83 ANSWER 1 OF 41 WPIX (C) 2002 THOMSON DERWENT

AN 2002-470759 [50] WPIX
DNC C2002-133790
TI Biomolecular **carriers** used for targeting drugs **carriers** to select tissues via the up-regulation of adhesion molecules expressed on endothelial cells, comprises biomolecule **carriers** bearing molecules binding to a **cellular adhesion molecule**.
DC B04 D16
IN GOETZ, D J; KIANI, M F
PA (GOET-I) GOETZ D J; (KIAN-I) KIANI M F; (UYTE-N) UNIV TENNESSEE RES CORP
CYC 87
PI US 2002044959 A1 20020418 (200250)* 1p A61K039-395 <--
WO 2002030456 A1 20020418 (200250) EN A61K039-00 <--
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SL SZ TR TZ UG ZW
W: AL AM AT AU AZ BA BB BG BR BY CA CH CN CU CZ DE DK EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT UA UG UZ VN YU ZA ZW
ADT US 2002044959 A1 Provisional US 2000-239666P 20001012, US 2001-975899 20011012; WO 2002030456 A1 WO 2001-US31881 20011012
PRAI US 2000-239666P 20001012; US 2001-975899 20011012
IC ICM **A61K039-00; A61K039-395**
ICS **A61K009-127**
AB US2002044959 A UPAB: 20020807
NOVELTY - A biomolecular **carrier** of pharmaceuticals (I), comprising a biomolecule **carrier** bearing molecules that bind to a **cellular adhesion molecule** expressed on endothelial cell and a pharmaceutical, is new.
DETAILED DESCRIPTION - An INDEPENDENT CLAIM is also included for a method of treating a pathophysiological state in an individual in need of such treatment, comprising irradiating a target tissue or organ in the individual, and administering to the individual (I).
ACTIVITY - Cytostatic; vasotropic; ophthalmological.
No supporting data is given.
MECHANISM OF ACTION - Drug **Carrier**.
In combined radiation/targeting therapeutic models, the ligand-bearing drug **carrier** is be administered subsequent to, or in conjunction with, the radiotherapy. The drug **carrier** contains a therapeutic agent (e.g. an organic compound, or a nucleic acid) and, on its outer surface, a recognition molecule (ligand) for a cognate molecule (receptor) that is expressed selectively (due to exposure to the radiation) on the lumenal surface of the endothelium within the irradiated tissue. These **carriers** bind predominately within the vasculature of the irradiated tissue (i.e. the cancerous tissue) and not bind to the vasculature of normal tissue. In this manner, the radiation-induced up-regulation of a endothelial **cell adhesion molecule**(s) within the diseased tissue is used as a target to deliver therapeutic agents (drugs, genes, etc.) selectively to the site of disease. In a series of experiments (n=4 animals), the adhesion of polystyrene microspheres coated with a monoclonal antibody to **ICAM -1** to irradiated (10 Gy single local dose of X-ray) cerebral microvasculature was investigated in a rat closed cranial window model. Fluorescent 2 micro m diameter microspheres coated with either rat anti-**ICAM-1** antibody or IgG (negative control) were injected via tail vein into rat bearing closed cranial windows. Dual color fluorescent microscopy was used to quantify the level of adhesion of anti-**ICAM-1** and IgG bearing microspheres to the cerebral venules before and after radiation. The results showed that in the irradiated tissue a large number of anti-**ICAM-1** coated microspheres adhere to the vessel wall, while very few IgG coated microspheres adhere to the walls of the same vessel. There was also very little adhesion of anti-**ICAM-1** coated microspheres to

the same vessels before this area of the brain was irradiated. The compiled data from the 4 animals revealed that the adhesion of anti-**ICAM-1** coated microspheres to the irradiated cerebral microvasculature is up to 25 times higher than control and reaches a peak 48 hours post-irradiation. The number of adhering antibody bearing microspheres to sham irradiated microvasculature did not significantly differ from control up to 7 days post-irradiation. Note that the enhanced adhesion of antibody bearing microspheres to the irradiated tissue in vivo was much more pronounced compared to the adhesion of antibody bearing microspheres in vitro. The presence of red cells in vivo, which have been shown to enhance the interaction of particles with the endothelium (52; 54), is the reason for this higher rate of adhesion. This can be shown in vitro with a flow chamber system using microspheres suspended in media containing red blood cells.

USE - The biomolecular **carrier** is used for targeting drugs (or gene) **carriers** to select tissues (especially cancerous tissues) via the up-regulation of adhesion molecules expressed on endothelial cells in response to exposure to radiation. The pathophysiological state treated is cancer, arteriovenous malformations (AVM), macular degeneration and restenosis (all claimed).

ADVANTAGE - It has been well established that the microvasculature of tissue exposed to ionizing radiation is significantly altered. These changes include an up-regulation of certain adhesion molecules on the lumenal surface of the endothelium. The radiation induced up-regulated expression of endothelial adhesion molecules provides an avenue for targeting drugs to select tissues. The prior art is deficient in the ability to target drug (or gene) **carriers** to select tissue via the up-regulation of adhesion molecules expressed on endothelial cells in response to exposure to radiation.

Dwg.0/0

FS CPI

FA AB; DCN

MC CPI: B04-F02; **B04-G01; B04-H20; B14-F02; B14-H01; B14-N03; B14-S03; D05-H10;** D05-H14B2

TECH UPTX: 20020807

TECHNOLOGY FOCUS - BIOTECHNOLOGY - Preferred Biomolecular **Carrier** : The molecules that bind to a **cellular adhesion molecule** are antibodies, antibody fragments and ligands that bind to the **cellular adhesion molecule**. The **carrier** is made from biodegradable particles, liposomes, microbubbles, polymersomes, and synthetic secretory granules. The **cellular adhesion molecule** is **ICAM** (undefined)-1, **E-selectin, P-selectin, VCAM** (undefined)-1, and **PECAM** (undefined)-1. The pharmaceutical is an anti-neoplastic compound. Preferred Method: The pathophysiological state is cancer, arteriovenous malformations (AVM), macular degeneration and restenosis. Preparation: (I) is prepared by coating the particles with protein A via passive adsorption, washed and incubated with a specific monoclonal antibody to an endothelial **cell adhesion molecule, ICAM-1**, and quantified via radiolabelling assays.

ABEX

EXAMPLE - Ligand coated polystyrene particles were prepared as follows. The particles were coated with protein A via passive adsorption. To achieve this, the particles were incubated in a 0.1M $NaHCO_3$, pH 9.2 buffer containing 300 microg/ml protein A at room temperature for over an hour. Following the adsorption, the particles are washed, incubated in a blocking buffer (Hank's balanced saline solution supplemented with 1% human or rat serum albumin), washed and incubated with a specific monoclonal antibody to an endothelial cell adhesion molecule diluted in blocking buffer. After a 1-hour incubation, the monoclonal antibody coated

particles are washed and stored in the blocking buffer prior to use in an assay. Particles coated with a monoclonal antibody to ICAM-1 (commercially available) were initially generated. The final surface density of the monoclonal antibody on the particles was controlled by altering the amount of monoclonal antibody used in the monoclonal antibody coating step. The surface density of monoclonal antibodies on the particles was quantified via radiolabelling assays. When working with microspheres, the washing steps (separation of the particles from solutions) were achieved via centrifugation and the concentration of microspheres in a solution is determined via a hemocytometer. When working with nanospheres, the separations are achieved via gel filtration and the concentration of nanospheres in a solution will be determined via absorbance readings and comparison to a standard curve as described. These methods are well established (Goetz, et al., J. Cell Biol. 137: 509-519, 1997) and allowed generation of ligand coated particles.

L83 ANSWER 2 OF 41 WPIX (C) 2002 THOMSON DERWENT
AN 2002-382792 [41] WPIX
DNC C2002-107821
TI Sustained release composition for treating e.g. multiple sclerosis, comprises microparticles containing an active agent, a biocompatible polymer and a water-soluble polymer.
DC A96 B04 D16
IN SCHER, D S; TRACY, M A
PA (ALKE-N) ALKERMES CONTROLLED THERAPEUTICS
CYC 97
PI WO 2002015877 A2 20020228 (200241)* EN 38p A61K009-00 <--
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SL SZ TR TZ UG ZW
W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK DM DZ EC EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ PH PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW
AU 2001085143 A 20020304 (200247) A61K009-00 <--
ADT WO 2002015877 A2 WO 2001-US26094 20010821; AU 2001085143 A AU 2001-85143 20010821
FDT AU 2001085143 A Based on WO 200215877
PRAI US 2000-644631 20000823
IC ICM **A61K009-00**
AB WO 200215877 A UPAB: 20020701
NOVELTY - A sustained release composition comprising microparticles containing an antigen or a labile agent, a biocompatible polymer and a water soluble polymer representing 20 % of the dry weight of microparticles, is new.
DETAILED DESCRIPTION - A new sustained release composition comprises microparticles containing an antigen or a labile agent, a biocompatible polymer and a water soluble polymer representing 20 % of the dry weight of microparticles, where the microparticles have a number median diameter of greater than 20 microns upon administration and generate pseudo-microparticles upon hydration having a number median diameter of less than 20 microns.
ACTIVITY - Immunosuppressive; Dermatological; Antiinflammatory; Neuroprotective; Antiviral; Antibacterial; Antiprotozoal; Antifungal; Antiallergic. No suitable biological data is given.
MECHANISM OF ACTION - Systemic immune response stimulator; Immune response modulator; Vaccine.
USE - The composition is used:
(i) for stimulating a systemic immune response to an antigen representing cell (e.g. dendritic cell or macrophage Kupffer cell, aveolar macrophage, microglial cell, splenic macrophage and/or macrophage in the Peyer's of the gut) in a mammal;
(ii) for the systemic delivery of a labile agent to a mammal; and
(iii) for modulating an immune response of the composition (all

claimed).

It is also used for the targeted delivery of biological active agents to specific tissue and cells and for treating autoimmune disease e.g. systemic lupus erythematosus and multiple sclerosis and treatment of conditions exacerbated by the activity of macrophages e.g. schistosomiasis.

ADVANTAGE - The composition provides the dissolution of the water-soluble polymer at a much greater rate than the degenerative of the biocompatible polymer. This variance in solubility generates pseudo-microparticles having a number mean diameter of at most about 20 (preferably at most 10 especially 1 - 5) microns which is substantially smaller than the size of the administered microparticles (number median diameter of at least 20 microns). The generation of pseudo-microparticles overcomes the problems associated with the processing and handling of small microparticles. A small delivery device is needed to obtain delivery of sufficient levels of the agent. A single dose of the composition is sufficient to result in long term and even permanent immunity to the incorporated antigen.

Dwg.0/2

FS CPI

FA AB; DCN

MC CPI: A12-V01; B04-B03C; **B04-B04C**; B04-C03; B04-H01; B04-H02; B04-H04B; B04-H04C; B04-H05; B04-H06; B04-H06F; B04-H08; B04-H09; B04-H13; B04-N04; B05-A01A; B05-A01B; B05-A03A; B07-A02A; B10-D01; B14-A01; B14-A02; B14-A03; B14-A04; B14-B03; B14-C03; B14-G01; B14-G02A; B14-J01; B14-J02; B14-N17C; B14-S01; B14-S11; D05-H07; D05-H10; D05-H18

TECH UPTX: 20020701

TECHNOLOGY FOCUS - PHARMACEUTICALS - Preferred Composition: The composition is enterically coated and further comprises a cytokine and a metal cation component dispersed within the biocompatible polymer.

TECHNOLOGY FOCUS - BIOLOGY - Preferred Components: The cytokine is selected from interleukin (IL)-1(alpha or beta), IL-2, IL-3, IL-4, IL-5, IL-6, IL-7, IL-8, IL-9, IL-10, IL-11, IL-12, granulocyte macrophage-colony stimulating factor (GM-CSF), M-CSF, leukemia inhibitory factor (LIF), leukotriene (LT), transforming growth factor (TGF)-beta, gamma-IFN (interferon), alpha-IFN, -beta-IFN, tumor necrosis factor (TNF)alpha, B Cell Growth Factors (BCGF), CD2 **ICAM** (**intercellular adhesion molecule**) MAdCAM or monocyte chemotactic protein (MCP)-1-3. The cytokine and antigen are co-incorporated into the microparticles or incorporated into separate microparticles. The separate microparticles are administered simultaneously or sequentially. The antigen is an allergen, viral antigen, bacterial antigen, protozoan antigen or a fungal antigen, (preferably influenza antigen, respiratory syncytial antigen, parainfluenza virus, helminthic pathogen antigen, Staphylococcus antigen, Hemophilius antigen or an antigen to vaccinate against allergies, especially a DNA-based vaccine, comprising plasmid DNA. The antigen is present at a concentration (w/w.%) of 0.01 - 50 (preferably 0.01 - 30). The labile agent is a protein, polypeptide or oligonucleotide (preferably a protein).

TECHNOLOGY FOCUS - POLYMERS - Preferred Polymer: The water-soluble polymer is a nonionic surfactant (preferably poloxamers, polysorbates, polyethyleneglycols and/or polyvinylpyrrolidones especially poloxamer 188 and/or poloxamer 407 or polysorbate 80 and/or polysorbate 20). The water-soluble polymer (%) is present in an amount at least 40 (preferably 40 - 60, especially 40 - 50). The biocompatible polymer is biodegradable and is selected from poly(lactide)s, poly(glycolide)s, poly(lactide-coglycolide)s, poly(lactic acid)s, poly(glycolic acid)s, poly(lactic acid-co-glycolic acid)s, poly(caprolactone), polycarbonates, polyestermide, polyanhydrides, poly(amino acid)s, poly(ortho esters)s, polycyanoacrylates, polyamides, polyacetals, poly(ether ester)s, copolymers of poly(ethylene glycol) and poly(ortho ester)s,

poly(dioxanone)s, poly(alkylene alkylate)s, biodegradable polyurethanes, blends and/or copolymers (preferably poly(lactide-co-glycolide).

TECHNOLOGY FOCUS - INORGANIC CHEMISTRY - Preferred Components: The labile agent is complexed to a stabilizing metal cation. The metal cation is selected from Zn+2, Ca+2, Cu+2, Mg+2 and/or K+. The metal cation component is dispersed within the biocompatible polymer and is selected form Mg(OH)2, MgCO3, CaCO3, ZnCO3, Mg(OAc)2, Zn(OAc)2, ZnSO4, MgCl2, ZnCl2, MgSO4, zinc citrate or magnesium citrate.
Preparation: The composition is produced by standard chemical techniques.

ABEX

SPECIFIC COMPOUNDS - Bordetella pertussis, Neisseria gonorrhea, Streptococcus pneumoniae and Plasmodium falciprum are specifically claimed as the antigen.

ADMINISTRATION - The composition is administered orally or parenterally (claimed) e.g. by inhalation or injection, implantation (e.g. subcutaneously, intramuscularly, intraperitoneally, intracranially or intradermally), intravaginally, intrapulmonary, bucally or by a suppository or by in situ delivery e.g. enema or aerosol spray.

EXAMPLE - Trehalose containing microparticles were prepared using a poly(lactide-Co-glycolide)(PLG) (10 w/v%) solution in methylene chloride in the polymer solution. A portion of microparticles were incubated for 2 hours at 37 degrees Centigrade in pH 7.2 phosphate buffered saline (sodium phosphate (50 mM), NaCl (100 mM), sodium azide (0.02 %)). The buffer was removed and the microparticles were dried by lyophilization. The pre-hydration and post-hydration particle size (micrometers) of the microparticles were 47.6 and 1.4 respectively.

L83 ANSWER 3 OF 41 WPIX (C) 2002 THOMSON DERWENT
AN 2002-179119 [23] WPIX
DNC C2002-055520
TI New immunogenic composition, useful for treating or preventing cancers or tumors, comprises tumor cell membrane preparation having glycosylated phosphatidylinositol-anchored co-stimulatory surface molecule.
DC B04 D16
IN SELL, K W; SELVARAJ, P
PA (SELL-I) SELL K W; (SELV-I) SELVARAJ P
CYC 1
PI US 2002009468 A1 20020124 (200223)* 39p A61K039-00 <--
ADT US 2002009468 A1 Provisional US 1996-23977P 19960815, US 1997-929464 19970815
PRAI US 1996-23977P 19960815; US 1997-929464 19970815
IC ICM **A61K039-00**
ICS A61K045-00; **A61K047-00**; C07H021-02; C07H021-04; C07K001-00; C07K014-00; C07K017-00
AB US2002009468 A UPAB: 20020411
NOVELTY - An immunogenic composition comprising:
(a) a tumor cell membrane preparation, where the tumor cell in nature lacks immunological co-stimulatory cell surface molecule (CoCAM), and membrane preparation has a glycosylated phosphatidylinositol (GPI)-anchored CoCAM protein stably incorporated into it; and
(b) a pharmaceutical **carrier**, is new.
DETAILED DESCRIPTION - An INDEPENDENT CLAIM is also included for preventing or ameliorating a neoplastic condition in an animal, by:
(1) preparing neoplastic cells or neoplastic cell membranes from cells of the neoplasm, where in nature, the neoplastic cells lack a CoCAM surface protein;
(2) preparing a CoCAM derivative protein having a GPI moiety which mediates insertion into a cell membrane to produce a GPI-CoCAM derivative preparation;
(3) incubating the neoplastic cell or cell preparation with the

GPI-CoCAM derivative under conditions allowing insertion of the GPI moiety of the GPI-CoCAM derivative into the neoplastic cell preparation or cell membrane preparation, to produce a GPI-CoCAM-modified neoplastic cell preparation or cell membrane preparation; and

(4) administering the GPI-CoCAM modified neoplastic cell preparation or cell membrane preparation to an animal in which protection from or amelioration of the neoplastic condition is needed.

ACTIVITY - Cytostatic. C57BL/6 mice were immunized with 100 micro liter total volume intraperitoneally with either HBSS (undefined), EG7 membranes or GPI-B7 incorporated EG7 membranes twice at a 2-week interval. Three weeks after the final immunization, spleens were harvested and T cell were purified using mouse T cell enrichment columns. Some mice were immunized as above, with the addition of IL-12 treatments in vivo. Treatment with EG7 membranes + GPI-B7 with or without IL-12 showed 0 out of 10 tumor incidence. There was 8/10 (-IL-12) and 10/10 (+IL-12) tumor incidence with HBSS, while a 7/10 (- IL-12) and 8/9 (+ IL-12) for EG7 membranes.

MECHANISM OF ACTION - Vaccine; immunotherapy.

USE - The immunogenic composition is useful for treating or preventing cancer and/or tumors, including carcinomas, sarcomas, leukemia, and lymphoma. The composition may also be used with hyperproliferative tissue, precancerous but neoplastic lesions, a single tumor, or metastatic tumors. The composition is especially useful for generating protective and/or therapeutic immune response, to prevent the establishment of a tumor and/or to result in regression of a previously established tumor.

Dwg.0/19

FS CPI

FA AB; DCN

MC CPI: B04-F02A; **B14-H01**; B14-S11C; D05-H07; D05-H14B2

TECH UPTX: 20020411

TECHNOLOGY FOCUS - BIOTECHNOLOGY - Preferred Method: In the prevention or amelioration of neoplastic condition, such as tumor, the GPI-anchored CoCAM is selected from a GPI-modified B7.1 or B7.2, a GPI-modified **intracellular adhesion molecule** (**ICAM**)**-1** or **ICAM**-2, a GPI-modified LFA-3, and a modified **VCAM-1**, preferably B7.1. The GPI-modified B7.1 derivative is a B7.1-CD16 fusion protein.

Preferred Composition: The GPI-anchored CoCAM is B7.1, and the GPI anchor is CD16, Decay Accelerating Factor, or LFA-3. The composition further comprises interleukin (IL) 6 or 12 and an immunological adjuvant.

ABEX

ADMINISTRATION - The composition is administered by injection, at a dose of 100-5000 microgram per dose.

EXAMPLE - A DNA fragment encoding the first 243 amino acids of human B7-1 was polymerase chain reaction (PCR)-amplified from the pT7 vector. The sense primer consisted of an oligonucleotide corresponding to nucleotides 300-323, including the 5' signal sequence and initiation codon of human B7-1 with a modification to include a Hind III restriction site. The antisense primer corresponded to nucleotides 1020-1043 of human B7-1 with the introduction of a Bcl I site at the B7-1 and CD16B joining site resulted in a conservative amino acid change from Leu to Val. The DNA fragment encoding the signal for glycosylated phosphatidylinositol (GPI)-anchor attachment of CD16B was PCR-amplified from a cDNA vector. The GPI anchor region from CD16B incorporated in the GPI-B7-1 fusion protein encompasses amino acids 193-234 of CD16B. the 2 amplified gene sequences were annealed to form a chimeric GPI-anchored B7-1 molecule by the overlap PCR method using 0.5 microgram each of the chimera was cloned in the shuttle vector TA, amplified in Escherichia coli DH5 alpha and subcloned in the neomycin-resistance plasmid pCDNA3 restriction sites. All end products were sequenced to be sure no further mutations had occurred as the result of the PCR manipulations. The chimeric gene was subcloned into the eukaryotic expression vector pCDNA3neo, and the resultant recombinant plasmid was transfected into Chinese hamster ovary (CHO) K1 cells using

the CuCl2 precipitation method, and transfectants were selected with G418 at 800 microgram/ml. Phosphatidylinositol-specific phospholipase C treatment was carried out to confirm that the B7-1 moiety was anchored to the cell surface by a GPI-anchor. Recombinant CHO cells were treated with 0.2 U/ml of PIPLC (undefined) for 1 hour at 37 degrees C, and the release of GPI-anchored molecules were monitored by fluorescence-activated cell sorting.

L83 ANSWER 4 OF 41 WPIX (C) 2002 THOMSON DERWENT
AN 2002-089788 [12] WPIX
DNN N2002-066188 DNC C2002-027658
TI New human monoclonal antibodies specific for dendritic cells, useful for inhibiting growth or inducing cytolysis of a dendritic cell and treating or preventing a dendritic cell mediated disease, e.g., autoimmune disorders.
DC B04 D16 P14 S03
IN DEO, Y M; KELER, T
PA (MEDA-N) MEDAREX INC
CYC 96
PI WO 2001085798 A2 20011115 (200212)* EN 95p C07K016-28
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SL SZ TR TZ UG ZW
W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK DM DZ EC EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW
AU 2001061383 A 20011120 (200219) C07K016-28
ADT WO 2001085798 A2 WO 2001-US15114 20010508; AU 2001061383 A AU 2001-61383 20010508
FDT AU 2001061383 A Based on WO 200185798
PRAI US 2000-230739P 20000907; US 2000-203126P 20000508
IC ICM C07K016-28
ICS A01K067-027; **A61K039-00**; A61K039-02; A61K039-12; **A61K039-395**; **A61K047-48**; A61P031-00; A61P035-00; A61P037-00; C07K016-46; C12N005-20; C12N015-63; G01N033-569; G01N033-577
AB WO 200185798 A UPAB: 20020221
NOVELTY - Isolated human monoclonal antibodies (I), or their antigen binding portions that specifically bind to dendritic cells, are new.
DETAILED DESCRIPTION - The isolated human monoclonal antibody (I) or its antigen binding portion has one or more of the following characteristics:
(a) a binding affinity constant to a dendritic cell of at least about 10 7 M-1;
(b) the ability to opsonize a dendritic cell;
(c) the ability to internalize after binding to dendritic cells; or
(d) the ability to activate dendritic cells.
The isolated human monoclonal antibody or its antigen binding portion may also have any of the following characteristics:
(a) mediates cytolysis of dendritic cells in the presence of human effector cells; or
(b) inhibits growth of dendritic cells.
(I) comprises a variable light chain having the sequence comprising 107 amino acids fully defined in the specification, and a variable heavy chain having the sequence comprising 116 amino acids fully defined in the specification. Furthermore, (I) or its antigen binding portion, binds to and blocks the human mannose receptor on dendritic cells. The antibody has a molecular weight of 36-40 kD as measured by polyacrylamide gel electrophoresis (PAGE) on human dermal dendritic cells, human epidermal dendritic cells, and dendritic cells derived from cynomolgus macaques.
INDEPENDENT CLAIMS are also included for the following:
(1) a hybridoma comprising a B cell obtained from a transgenic non-human animal having a genome comprising a human heavy chain transgene

and a light chain transgene fused to an immortalized cell, where the hybridoma produces a detectable amount of (I);

(2) a transgenic non-human animal, which expresses (I), where the transgenic non-human animal has a genome comprising a human heavy chain transgene and a human light chain transgene;

(3) producing (I);

(4) bispecific molecules comprising:

(a) at least one first binding specificity for dendritic cells and a second binding specificity for an Fc receptor; or

(b) at least one first binding specificity for dendritic cells and a second binding specificity for an antigen on a target cell;

(5) compositions comprising:

(a) the isolated human monoclonal antibody or its antigen-binding portion and a pharmaceutical **carrier**; or

(b) a combination of two or more isolated human antibodies or antigen-binding portions, where each of the antibodies or antigen-binding portions binds to a distinct epitope on a dendritic cell;

(6) inhibiting growth of a dendritic cell comprising contacting a dendritic cell with (I) or its antigen-binding portion;

(7) inducing cytolysis of a dendritic cell comprising contacting a dendritic cell with (I) or its antigen-binding portion that specifically binds to dendritic cells in the presence of an effector cell, such that cytolysis of the dendritic cell occurs;

(8) treating or preventing a dendritic cell mediated disease by administering (I) or its antigen binding portion;

(9) detecting the presence of a dendritic cell in a sample comprising:

(a) contacting the sample and a control sample, with (I) or its antigen binding portion to allow the formation of a complex between the antibody or its portion and the dendritic cell; and

(b) detecting the formation of a complex, where a difference complex formation between the sample compared to the control sample is indicative the presence of dendritic cell in the sample;

(10) an expression vector comprising a nucleotide sequence encoding a variable and constant region of the heavy and light chains (I) or its antigen binding portion;

(11) targeting an antigen to a dendritic cell in a subject by administering (I) or its antigen binding portion, which is operably linked to an antigen, such that antigen is targeted to the dendritic cell;

(12) a molecular complex comprising:

(a) at least one binding specificity for a component on the surface of a dendritic cell; and

(b) at least one antigen linked to the binding specificity, where the component mediates internalization of the molecular complex when bound by the binding specificity;

(13) inducing or enhancing an immune response against an antigen in a subject comprising administering to the subject the molecular complex;

(14) immunizing a subject comprising administering to the subject the molecular complex;

(15) targeting a cell to a dendritic cell; and

(16) preventing binding of a pathogen to human mannose receptor on dendritic cells by contacting (I) or its antigen binding portion with dendritic cells to prevent binding of the pathogen to the cells.

ACTIVITY - Immunomodulatory; antiinflammatory; antirheumatic; antiarthritic; neuroprotective; antidiabetic; antianemic; endocrine; dermatological; antithyroid; uropathic; opthalmological; muscular.

No supporting data given.

MECHANISM OF ACTION - Dendritic cell modulator.

The antibody B11 conjugated to tetanus toxoid (TT) or TT alone was added at various concentrations to dendritic cells. Autologous TT-specific T cells were added to each well containing dendritic cells at 50 000 cells per well. Cells were cultures together for 7 days at 37 deg. C and assayed for the number of living cells using a 3-(4,5-dimethylthiazol-2-yl)-2,5-

diphenyl tetrazolium bromide (MTT) based assay. The ability to induce dendritic cells to specifically stimulate TT-specific T lymphocytes was compared after exposing cells to TT or antibody B11-TT. The results showed that conjugating TT as a model antigen to B11 leads to more efficient antigen presentation as measured by antigen-specific T cell proliferation. T-cell stimulation index for B11-TT was (approximate values) 3.5, 2.1, 1.4, 1.2 and 1.1 at an antigen concentration of 10, 1, 0.1, 0.01 and 0.001 micro g/ml respectively, compared to (approximate values) 1.6, 1.2, 0.9, 1.1 and 1.0 for TT alone at the same antigen concentrations, respectively.

USE - (I) or their antigen-binding fragments are useful for inhibiting growth of a dendritic cell, inducing cytolysis of a dendritic cell, treating or preventing a dendritic cell mediated disease, detecting the presence of a dendritic cell, targeting an antigen to a dendritic cell and preventing binding of a pathogen (a virus or a bacterium) to human mannose receptor on dendritic cells. In particular, (I) may be used to treat, e.g., autoimmune disease or graft versus host disease (all claimed).

Furthermore, (I) may also be useful for treating immune system or inflammatory disorders (e.g., rheumatoid arthritis), multiple sclerosis, diabetes mellitus, myasthenia gravis, pernicious anemia, Addison's disease, lupus erythematosus, Reiter's syndrome, and Graves disease.

Dwg.0/13

FS CPI EPI GMPI

FA AB; DCN

MC CPI: **B04-B04C1**; **B04-B04C2**; B04-E08; B04-F04; B04-F05; B04-G06; B04-G21; B11-C08E; B12-K04E; B14-C03; B14-C09B; B14-F03; B14-G02C; B14-G02D; B14-G03; B14-J05; **B14-N03**; B14-N11; B14-N17; B14-S01; B14-S04; D05-C12; D05-H09; D05-H11A1; D05-H12E; D05-H15; D05-H16A

EPI: S03-E14H4

TECH UPTX: 20020221

TECHNOLOGY FOCUS - BIOTECHNOLOGY - Preparation: (I) is prepared by a method comprising:

(a) immunizing a transgenic non-human animal having a genome comprising a human heavy chain transgene and a human light chain transgene with dendritic cells, such that antibodies are produced by B cells of the animal;

(b) isolating B cells of the animal; and

(c) fusing the B cells with myeloma cells to form immortal, hybridoma cells that secrete human monoclonal antibodies specific for dendritic cells (claimed).

Preferred Antibody: The isolated human antibody or its antigen binding portion has an isotype consisting of IgG1, IgG2, IgG3, IgG4, IgM, IgA1, IgA2, IgAsec, IgD and IgE, preferably an IgG1kappa. (I) or its antigen binding portion binds to an antigen present of the cell surface of a dendritic cell, particularly to the macrophage mannose receptor and is produced by a hybridoma, which includes a B cell obtained from a transgenic non-human animal having a genome comprising a human heavy chain transgene and a human light chain transgene fused to an immortalized cell. In particular, the hybridoma is selected from A3, A5, A23, A24, A33, B9, B11, B33, B47, C8, C10, C20, C28, C29, C30, C35, E1, E8, E10, E18, E20, E21 and E24.

The isolated human antibody or its antigen binding portion is capable of mediating cytolysis of dendritic cells by human effector cells at an IC50 of 1 x 10-7 M or less in vitro. In addition, (I) may be conjugated to a binding specificity for a Fc receptor, a cytotoxin or to an immunomodulatory compound.

Moreover, (I) induces cytokine release by dendritic cells or modulates the expression of immunomodulatory receptors on the surface of dendritic cells. The immunomodulatory receptor is selected from CD80 (B7.1), CD86 (B7.2), CD40, and CD54 (**ICAM**).

Preferred Method: In the method of (13), the immune response comprises antibodies that bind to the antigen, or T cells that bind to the antigen

as a component of an MHC-I or MHC-II complex. In method (15), targeting a cell to a dendritic cell comprises linking a human monoclonal antibody or its antigen binding portion to the surface of a cell, such that the cell is targeted to a dendritic cell. It may also comprise transfecting a cell with a nucleic acid molecule encoding a human monoclonal antibody or its antigen binding portion, such that the cell expresses the antibody or antigen binding fragment on the surface of the cell, thereby targeting the cell to a dendritic cell.
Preferred Molecule: The Fc receptor is a human FcgammaRI or a human Fcalpha receptor. The bispecific molecule binds to the Fc receptor at a site, which is distinct from the immunoglobulin binding site of the receptor. The molecular complex has one or more the binding specificities comprising an antibody consisting of A3, A5, A23, A24, A33, B9, B11, B33, B47, C8, C10, C20, C28, C29, C30, C35, E1, E8, E10, E18, E20, E21 and E24, or their antigen binding fragments. The antigen is selected from a tumor antigen, a microbial antigen, a viral antigen, and an autoantigen. The antigen is chemically linked to the binding specificity or is recombinantly fused to the binding specificity.

ABEX

ADMINISTRATION - Administration is oral, nasal topical (e.g., buccal and sublingual), rectal, vaginal or parenteral (e.g., intravenous, intramuscular, intraarterial, intrathecal, intracapsular, intraorbital, intracardiac or intradermal).
No dosage given.
EXAMPLE - Human anti-dendritic cell monoclonal antibodies were generated by immunizing the HCO7 strain HuMAb mice with preparations of dendritic cells. Human peripheral blood mononuclear cells (PBMCs) were obtained by density gradient centrifugation of whole blood. Monocytes were isolated by adherence to tissue culture flasks for two hours, and then differentiated into dendritic cells. Cells for immunization were used fresh or stored frozen at -80 degreesC. Mice were immunized every 2-3 weeks. Finally, an intravenous injection of dendritic cells in phosphate buffered saline (PBS) was performed prior to splenectomy. The spleens from responding mice were harvested and dispersed into single cells.
To generate hybridomas producing anti-dendritic cell antibodies, splenocytes from mice with plasma containing anti-dendritic cell antibodies were fused with P3X63-Ag8.653 myeloma cells (ATCC CRL 1580) and PEG. Hybridomas were selected by growth in HAT containing media.
After hybridomas grew out, each well containing hybridomas was screened for the production of human IgG using an anti-human IgG ELISA. Positive hybridomas were screened for and selected based on the following properties: (1) production of human IgG antibodies, and (2) binding to dendritic cells.
The hybridomas screening human IgG were tested for creativity with various types of blood cells by flow cytometry.
Dendritic cells were prepared from adherent mononuclear cells by culturing for 5-7 days in media supplemented with GM-CSF and IL-4. Granulocytes (PMN), monocytes and lymphocytes were obtained from heparanized whole blood. The cells were incubated with hybridoma supernatants from IgG-positive clones at 4C. Several hybridomas that were screened produced human IgG1kappa antibodies that demonstrated reactivity with dendritic cells as assessed by flow cytometry.

L83 ANSWER 5 OF 41 WPIX (C) 2002 THOMSON DERWENT
AN 2002-074870 [10] WPIX
DNC C2002-022185
TI Composition for inducing thrombus formation, useful for treating cancer, contains a binding agent having a region which binds to platelets.
DC B04 D16
IN NOUJAIM, A; PERSON, R H; STEWART, M W
PA (NOVO-N) NOVOLYTICS INC
CYC 88
PI WO 2000029029 A1 20000525 (200210)* EN 36p A61K047-48 <--

RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW NL
OA PT SD SE SL SZ TZ UG ZW
W: AE AL AM AT AU AZ BA BB BG BR BY CA CH CN CU CZ DE DK EE ES FI GB
GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU
LV MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR
TT UA UG US UZ VN YU ZA ZW
EP 1131106 A1 20010912 (200242) EN A61K047-48 <--
R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT
RO SE SI

ADT WO 2000029029 A1 WO 1999-IB1809 19991110; EP 1131106 A1 EP 1999-972110 19991110, WO 1999-IB1809 19991110

FDT EP 1131106 A1 Based on WO 200029029

PRAI US 1998-108129P 19981112

IC ICM **A61K047-48**
ICS **A61K039-395**

ICI A61K038:36, A61K038:48, A61K038:57, **A61K039:395**;
A61K039-395; **A61K039-395**; **A61K039-395**;
A61K038:57; A61K038:48; A61K038:36

AB WO 200029029 A UPAB: 20020213
NOVELTY - A composition for inducing thrombus formation, comprising a binding agent having a component which binds the agent to a pre-determined site, and a component which binds the agent to a platelet, is new.
DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following:
(1) a method of inducing thrombus in vivo, comprising:
(a) capturing platelets at a selected site;
(b) inducing activation of platelets; and
(c) allowing a thrombus to form.
(2) a kit for inducing thrombus formation comprising a binding agent for targeting a pre-determined site and at least one of: a binding agent for binding platelets, a ligand for binding the binding agent, a ligand conjugate, an anti-ligand for binding the ligand or it's conjugate, a platelet binding enhancer, a thrombus formation modulator, a complement cascade component, a complement cascade component inducer, and a binding agent for binding platelets that includes an anti-ligand.
ACTIVITY - Coagulant; Cytostatic.
No biological data is given.
MECHANISM OF ACTION - None given.
USE - For inducing thrombus formation in vivo (claimed), useful for treating cancer.
Dwg.0/0

FS CPI

FA AB; DCN

MC CPI: B04-B04D2; B04-C01; B04-C02E1; B04-C02E2; B04-E01; B04-G06; B04-H19; **B04-H20**; B04-H20A; B04-H20B; B04-N08; B05-B02C; B14-F08; **B14-H01**; **B14-H01B**; D05-H11

TECH UPTX: 20020213
TECHNOLOGY FOCUS - PHARMACEUTICALS - Preferred Composition: The pre-determined site binding component is an antigen binding site, preferably an antibody, monoclonal antibody, polyclonal antibody, humanized monoclonal antibody, chimeric antibody, single chain antibody, dimeric single chain antibody construct, a multimeric single chain antibody construct, a peptide, a nucleic acid, a protein, a ligand, an oligonucleotide, conjugates including them, fragments of them, functional equivalents of them, or more preferably a neo-epitope. The platelet binding component is von Willebrand factor, osteopontin, fibrinogen, fibrin, fibronectin, vitronectin, collagen, thrombospondin, laminin, heparin, heparan sulfate, chondroitin sulfate, phospholipase A2, matrix metalloproteinase, thrombin, glass, sialyl-lewis X, fibulin-1, **PECAM**, **ICAM-1**, **ICAM**-2, **p-selectin** ligand, MAC-1, LFA-1, or fragments or functional equivalents of them. The composition further comprises a platelet binding enhancer, preferably ristocetin, platelet microparticles, or platelet

membrane portions. The composition may include a thrombus formation modulator, preferably an inhibitor of fibrinolysis, an inhibitor of anti-coagulant protein, or tissue factor pathway inhibitor. The anticoagulant protein is protein C, protein S or antithrombin III. The fibrinolysis inhibitor is plasminogen activator inhibitor.
Preferred Method: Inducing platelets to collect at a pre-determined site comprises administering a targeting agent that specifically binds platelets. Claims 14-20 (page 31) related to the novel method are unavailable from the patent offices.
Preferred Kit: The binding agent for targeting a pre-determined site includes a binding component for binding platelets, or a ligand.

ABEX

WIDER DISCLOSURE - Disclosed as new are the following:
(1) compositions and methods for capturing platelets at a pre-determined site, activating the platelets, and harnessing the natural function of platelets;
(2) compositions and methods for indirectly treating a disease or condition by disrupting blood flow to a site;
(3) targeting platelets to a pre-determined tissue; and
(4) compositions and methods for treating cancer by inducing platelets to collect at a pre-determined site.

ADMINISTRATION - The composition is administered systemically, locally, orally or topically. No dosage is suggested.

EXAMPLE - No relevant example is given.

L83 ANSWER 6 OF 41 WPIX (C) 2002 THOMSON DERWENT
AN 2002-055316 [07] WPIX
DNN N2002-040789 DNC C2002-015787
TI New artificial antigen presenting cell, useful for modulating T cell response for treating allergies and cancers, comprises liposome, major histocompatibility complex, antigen and accessory molecule components.
DC B04 D16 S03
IN ALBANI, S
PA (ALBA-I) ALBANI S
CYC 90
PI WO 2001080833 A1 20011101 (200207)* EN 185p A61K009-127 <--
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW NL OA PT SD SE SL SZ TZ UG ZW
W: AE AL AM AT AU AZ BA BB BG BR BY CA CH CN CU CZ DE DK DM DZ EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW
AU 2000043137 A 20011107 (200219) A61K009-127 <--
ADT WO 2001080833 A1 WO 2000-IT161 20000420; AU 2000043137 A AU 2000-43137 20000420, WO 2000-IT161 20000420
FDT AU 2000043137 A Based on WO 200180833
PRAI WO 2000-IT161 20000420
IC ICM **A61K009-127**
ICS **A61K047-48**; C07K014-705; G01N033-569
AB WO 200180833 A UPAB: 20020213
NOVELTY - An artificial antigen presenting cell (I) comprising liposome (C1), major histocompatibility complex (MHC) (C2), antigen (C3) and accessory molecule components (C4), where C3 is in contact with C2, C2 and C4 are in contact with C1, and C4 further provides for a stabilizing property to an interaction between a T cell receptor (TCR) and C2 and C3, is new.
DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following:
(1) making (I);
(2) identifying (M1) T cells specific for an antigen of interest;
(3) isolating (M2) T cells specific for an antigen of interest;

(4) modulating (M3) T cell response;

(5) characterizing (M4) the functional state of antigen-specific T cells;

(6) treating (M5) a condition in a subject which would be benefited by altering the functional pattern of cytokine production by certain antigen-specific T cells to increase T-helper (Th) 2 response and/or decrease Th1 response;

(7) identifying (M6) antigen-specific T cells specific for epitopes on a graft donor's tissue likely to elicit graft versus host rejection response;

(8) treating (M7) a recipient mammal to reduce rejection of allografts in a transplantation therapy regime;

(9) a kit (II) for isolation and/or modulation of T cells specific for an antigen of interest comprising (I), solid supports, reagents and an immunomodulatory column device;

(10) an immunomodulatory column comprising a multiplicity of compartments positioned in relation to one another in series, the compartments having channels interconnecting adjacent compartments, where:

(a) the channels further have an unit to isolate the compartments from one another;

(b) the compartments further have one entrance and at least an exit port for receiving or expelling, respectively, a flowable medium; and

(c) the ports further have an unit to close the ports to impede the flowable medium; and

(d) the compartments further optionally comprise solid supports and artificial antigen presenting cells (APCs);

(11) identifying (M8) a gene which is expressed by a T cell specific for an antigen of interest, comprising:

(a) obtaining a biological sample containing T cells which are specific for an antigen of interest, labeling with a first label, at least the intracellular gene product of interest produced by T cells in the biological sample;

(b) preparing a liposome:MHC:antigen complex, where the antigen in liposome:MHC:antigen complex is antigen of interest, contacting the labeled biological sample with liposome:MHC:antigen complex to form liposome:MHC:antigen:T cell complex;

(c) labeling with a second label, the liposome:MHC:antigen:T cell complex; and

(d) discriminating according to antigen specificity, cells producing the intracellular gene product of interest, which cells have both the first label and the second label; and

(12) obtaining a monoclonal population of T cells specific for an antigen of interest;

(13) monitoring an immunological outcome of intervention on antigen-specific and bystander T cells, involves identifying antigen-specific T cells that are specific for an antigen of interest from a patient, identifying a functional phenotype of the identified antigen-specific T cells and correlating the functional phenotype with a clinical outcome of the patient.

ACTIVITY - Antidiabetic; neuroprotective; antirheumatic; antiarthritic; dermatological; immunosuppressive; ophthalmological; antiallergic; cytostatic; virucide; antibacterial. No supporting data is given.

MECHANISM OF ACTION - Increases Th-2 response and/or decreases Th-1 response; increases Th-1 response and/or decreases Th-2 response; T cell response modulator.

USE - (I) is useful for identifying T cells specific for an antigen of interest, isolating T cells specific for an antigen of interest and modulating T cell response. M4 is useful for characterizing the functional state of antigen-specific T cells. M5 is useful for treating autoimmune disease such as type I diabetes mellitus, multiple sclerosis, rheumatoid arthritis, dermatomyositis, juvenile rheumatoid arthritis or uveitis. Alternatively it is useful for treating allergy due to allergens such as

dust, animal skin bypass products, vegetables, fruits, pollen or chemicals, cancer, viral infection, bacterial infection. M6 is useful for identifying antigen-specific T cells specific for epitopes on a graft donor's tissue likely to elicit graft versus host rejection response. M7 is useful for treating a recipient mammal to reduce rejection of allografts in transplantation therapy regime. M8 is useful for identifying a gene expressed by a T cell specific for an antigen of interest. M9 is useful for obtaining a monoclonal population of T cells specific for an antigen of interest.

ADVANTAGE - Addition of the accessory molecules, as well as co-stimulatory molecules, and other proteins in proper orientation in the liposomes allow for substantially improved binding association and manipulation of T cells which is very important in the identification and stimulation of antigen-specific T cells. The use of co-stimulatory, adhesion and other accessory molecule in a free floating format also helps to both anchor and direct the interaction between MHC:antigen:accessory molecule and T cell receptors by providing a means by which T cells in the sample will be presented with a structure more similar to that found in the natural state. Since the artificial APCs may incorporate irrelevant molecules to be used in conjunction with separate solid support-based capture moieties for capturing generic target motifs such as irrelevant molecules, the system avoids a need for manufacturing specialized solid phase capture substrates for each antigen-specific complex, because of the capacity for the functional molecules to migrate in the liposome, the irrelevant molecules are nonspecifically directed away from the binding position of the T cells thus avoiding steric hindrances. Greater specificity in APC:T cell interaction is provided since the antigen is labeled rather than the MHC component. The consequence is a greater ability to bind, to stimulate, and modulate T cells on demand. Isolation and expansion of T cells specific for a particular antigen will increase the specificity and effectiveness of adoptive immunotherapeutic approaches.

Dwg.0/30

FS CPI EPI

FA AB; DCN

MC CPI: B01-D02; B04-B04D4; B04-B04D5; B04-E03F; B04-E05; B04-F01; B04-F04; **B04-G01**; B05-B02C; B06-A01; B06-A02; B06-F03; B11-C07B3; B11-C07B5; B11-C08B; B12-K04A; B14-A01; B14-A02; B14-C06; B14-C09B; B14-G02A; B14-G02C; B14-G02D; **B14-H01**; **B14-N03**; B14-N17; B14-S01; **B14-S03**; B14-S04; D05-H08; D05-H09; D05-H11; D05-H12A

EPI: S03-E14H4

TECH UPTX: 20020213

TECHNOLOGY FOCUS - BIOTECHNOLOGY - Preparation: (I) is produced by obtaining an MHC:antigen complex of interest, contacting MHC:antigen complex with a lipid and cholesterol and forming a lipid membrane-associated MHC:antigen complex and contacting the membrane-associated MHC:antigen complex with a molecule of interest such as an accessory molecule, co-stimulatory molecule, cell modulation molecule, adhesion molecule, irrelevant molecule, cholesterol, GM-1 protein, cholera toxin beta subunit protein or a label. Preferably, the second and third step of the method are performed simultaneously. Preferred Cell: In (I), (C1) comprises a lipid such as phospholipid, neutral phospholipid and a phosphotidylcholine, and (I) further comprises a surfactant components, such as cholesterol which is in contact with (C1). A label such as biotin, vancomycin, fluorochrome, fluoroscein isothiocyanate (FITC) or a radiolabel, is associated with a lipid bilayer or a lipid of (C1), or with (C2), (C3) or (C4). (C2) is a natural MHC, a recombinant MHC having sufficient composition for binding an antigen, an alpha 1- and alpha 2 subunit set of a class 1 MHC, alpha 1, beta 2 subunit set of a class II MHC, a peptide derived from the alpha and beta subunits, or a portion of a natural MHC having sufficient composition for binding an antigen. The antigen is presented by (C2) for contact with and recognition

by a TCR, where the antigen is a peptide, a peptide derived from the recipient for graft versus host disease, a cancer cell-derived peptide, a peptide derived from an allergen, a donor-derived peptide, a pathogen-derived molecule, a peptide derived by epitope mapping, self-derived molecule, a self-derived molecule that has sequence identity with the pathogen-derived antigen, the sequence identity being in the range of 5-100%, 15-100%, 35-100% or 50-100%. (C4) is lymphocyte function associated antigen (LFA)-1, CD11a/18, CD54 (**intercellular adhesion molecule** (**ICAM**)-**1**), CD106 (**vascular cell adhesion molecule** (**VCAM**)) or CD49d/29 (very late antigen 4 (VLA-4)) and antibodies to the ligands of the foregoing molecules. (I) further comprises a GM-1 protein components which are in contact with (C1), and cholera toxin beta subunit components which are connected to at least one of (C2) and (C4) and further contacts the GM-1 components. (I) further comprises co-stimulatory molecule components, an adhesion molecule components, cell modulation molecule components, GM-1 protein components, cholera toxin beta subunit components, an irrelevant molecule component (C5-C10) for binding (I) to a solid support or binding label or a label components. The label as described above, thus is associated with any of (C1-C10). Preferably, (C8) contacts at least (C1) and (C9) is connected to each of (C5), (C6), (C7), (C10) and further contacts (C8). (C5) is B7-1, B7-2, CD5, CD9, CD2, CD40 and antibodies to their ligands. (C6) is **ICAM -1**, **ICAM**-2 GlyCAM-1, CD34, anti-LFA-1, anti-CD44, anti-beta 7, chemokines, CXCR4, CCR5, anti-**selectin** L, anti-**selectin E** or anti-**selectin P**. (C7) is CD72, CD22, CD58, anti-CD22, anti-CD58, anti-CD72, anti-cytokine receptor, or anti-chemokine receptor. (C10) has a moiety for binding a solid support either directly or through an intermediate molecule, or for binding a label. The solid support is a glass or magnetic bead of 25-300 mum diameter. The solid support is preferably coated with phospholipid, a neutral phospholipid, phosphotidylcholine, and further comprises capture molecules that have the capacity to bind to (C10). The capture molecules are non-covalently associated with the lipid. (I) most preferably comprises (C1-C4), (C5) and/or (C7), where the (C2) and (C5) and/or (C7) molecules are in contact with at least (C1). Alternately, (I) comprises (C1-C7), (C10) and cholesterol component, where (C3) is in contact with (C2), and (C2), (C4), (C5-C7), (C10) and cholesterol components are in contact with (C1), and (C4) further provides a stabilizing property to an interaction between TCR and (C2) and (C3). Optionally, (I) comprises solid support component, (C1-C4), where the solid support comprises a glass or magnetic spheroid, and (C1) is contacted either covalently or noncovalently with the solid support component, in which case (I) further comprises (C5), (C6), (C7), (C8), (C9) and (C10) for binding the APC to a solid support or binding a label, and label components.

Preferred Kit: (II) comprises artificial APCs having components in any combination, the components being lipids, neutral phospholipids, phosphotidyl choline, cholesterol, solid supports, full length MHC components or its portion sufficient to bind an antigen, where the MHC components are specific for an antigen, antigens, accessory molecules, co-stimulatory molecules, adhesion molecules, modulation molecules, irrelevant molecules and labels. The antigen preferably has a label, and the irrelevant molecule components have a label and a moiety for binding a solid support either directly or through an intermediate molecule, or for binding a label. The lipid of the liposome also has a label, where the label is associated with lipid layer of the liposome. The reagents comprised in (II) comprise components such as buffers for carrying out T cell identification, isolation and modification, media for expanding T cells, costimulatory molecules, adhesion molecules, modulation molecules, labels, soluble factors for activating T cells and soluble factors for modulating T cells, in any combination.

Preferred Method: M1 comprises obtaining a T cell containing biological sample which are specific for an antigen of interest, preparing (I), where

the antigen in (I) is the antigen of interest, contacting the biological sample with (I) to form (I):T cell complex, where at least one element (an antigen of interest, an irrelevant molecule, a lipid bilayer, (C2), (C4), (C5), (C6), (C7)) of (I) is associated with a label and detecting the label. M2 comprises obtaining a biological sample containing T cells which are specific for an antigen of interest, preparing (I), where the antigen in (I) is antigen of interest, contacting the biological sample with (I) to form (I):T cell complex, where at least one element of (I) as described above is associated with a label, removing (I):T cell complex from the biological sample and separating T cells specific for antigen of interest from (I):T cell complex. The method further involves determining quantity of T cells specific for antigen of interest, and characterizing the functional phenotype of the isolated T cells specific for the antigen of interest. The biological sample used in the method is whole blood, blood cells, blood plasma or tissue. M3 comprises isolating T cells which are specific for antigen of interest by M2, and contacting the isolated T cells with (I) that has an antigen of interest or its homologue and further comprising (C4), (C5), (C6) and (C7). The modulation of T cell response involves changing in whole or in part the functional pattern of cytokine production by the isolated T cells from a Th-1 response to a Th-2 response, where (I) expresses co-stimulatory molecule B7-1 or anti-CD28 so as to facilitate T-cell proliferation, induction of T-cell proliferation or anergy. Optionally, the modulation of T-cell response involves changing in whole or in part, the functional pattern of cytokine production by isolated T cells from Th-2 response to a Th-1 response, where (I) expresses a co-stimulatory molecule B7-1. M3 comprises isolating T cells by M2, extracting mRNA from the isolated T cells, obtaining cDNA corresponding to the extracted mRNA, evaluating the mRNA encoding proteins that govern function and phenotype of the antigen-specific T cells, evaluation being carried out by mRNA translation of the proteins and testing the proteins using antibodies against such proteins. Alternatively by reverse transcriptase (RT)-PCR of the mRNA using primers specific for the proteins. Preferably, the evaluation of the mRNA encoding proteins that govern function and phenotype of the antigen-specific T cell is used to determine efficacy of an immunomodulation treatment regimen that comprises administering a vaccine, inducing tolerance in autoimmunity, reducing allergic response, or inducing immune response against cancer cells. The proteins that govern the function of the phenotype of the antigen specific T cells include a cytokine, chemokine, a chemokine receptor or a cytokine receptor. M5 comprises isolating T cells by M2 which are specific for an antigen capable of triggering an Th-1 or Th-2 response upon recognition by the antigen of the subject's T cells and combining the isolated T cells with (I) having a MHC component capable of binding the antigen and a co-stimulatory molecule component comprising B7-1 or B7-2, respectively. M6 comprises predicting epitopes of a donor's MHC likely to be antigenic by computer modeling and testing the predicted epitopes with a recipient's T cells to identify T cells specific for the epitopes according to M1. M7 comprises preparing (I) according to M1, using the epitopes tested as antigen in an artificial APC and contacting the artificial APC with the biological sample from the recipient to form artificial APC:epitope specific T cell complex, the sample further comprising T cells specific for the epitopes, removing the complex from the biological sample so as to deplete a recipient's T cell population of T cells for the epitope. In M8, the first and second labels are biotin, fluorochrome, fluoroscein isothiocyanate (FITC), or a radioactive label, provided that the first and second label or not the same. M9 comprises isolating T cells specific for an antigen of interest by M2, culturing the T cells in an individual well with the antigen of interest and an artificial APC.

ABEX

WIDER DISCLOSURE - Identifying antigenic motifs of pathogens that are recognized by the MHC is also disclosed as new.

ADMINISTRATION - No specific administration details are given.

EXAMPLE - Liposome assay was carried out for detection of antigen-specific cells. The capacity of T cells to bind to liposomes containing cholesterol having major histocompatibility complex (MHC):antigen complexes inserted into the liposome membrane was determined by flow cytometry analysis (FACS). Discrimination between antigen-specific T cells was facilitated by use of two T cell hybridomas specific for the same peptide. These hybridomas were OVA323-336 (which correspond to residue 323-326 of ovalbumin), which were restricted by two different MHCs, I-As and I-Ad. The designations for the restriction were I-As restricted OVA323-336 specific T cell hybridoma, AG111.207, and the I-Ad restricted OVA323-336 specific T cell hybridoma 8D051.15. A peptide containing 2 identities and one conservative substitution, HBi15 which correspond to residues 15-31 of a Hemophilus influenzae isoleucyl tRNA transferase, was used as a negative control. Liposomes were prepared similarly to that described by Brian et al., PNAS, 81:6159-63. Complexes of affinity-purified MHC molecules I-As and I-Ad were inserted into liposomes. The OVA323-336 peptide and the control peptide, Hi15, were biotinylated and the biotinylated peptides (b-peptides) were incubated with the liposome:MHC complexes for 18 hours at room temperature at a physiologic pH to from liposome:MHC:b-peptide complexes. These complexes were incubated with streptavidin fluoroscein isothiocyanate (FITC), and then with a standard amount of AG111.207 or 8D051.15 cells. When analyzed by flow cytometry, nearly 90% of the AG111.207 and 87.2% of 8D051.15 cells strained positive when using the correct restriction and peptide. The specificity of the entire interaction was demonstrated by lack of staining of AG111.207 and 8D051.15 cells when incubated with anti-CD4 antibody (Ab) and complexes of the incorrect restriction for each hybridoma, I-Ad and I-As respectively, and Hi15 which was two identities (p2,p10) and one conservative substitution (p5) with OVA323-336. The binding between MHC:b-peptide complexes and AG111.207 T cells was also concentration dependent. Only 13.1% of AG111.207 cells tested positive when the I-As/OVA323-336 concentration in the assay was reduced five fold to 13 microgram/ml. The signal was also reduced by the addition of 300 microgram/ml of the same, non-biotinylated OVA323-336 peptide as a competitive inhibitor during preparation of the I-As /OVA complexes (5.1% of CD4+ cells positive). The finding suggested that biotinylation of the peptide does not interface with the trimolecular interaction among peptide, MHC and T cell receptor (TCR). Also no binding to TCR-negative cells, such as B cell hybridoma HT.01, was detected (0% of cell positive). Using biotinylated I-Ad in liposomes without peptide, 6.9% of 8D051.15 cells bound the MHC alone. Hence, the interaction requires the presence of the specific peptide. Also the capability of (I)s (APC), was evaluated presenting synthetic biotinylated peptide OVA in the context of IAd, to visualize by FACS analysis hybridoma 8D0, which is OVA/IAd specific. The percentage of hybridoma cells was visualized by binding with cytochrome-tagged artificial APC. This interaction was specific, in so far as TCR binding was dependent on the availability of the MHC/peptide complexes. The interaction was inhabitable by addition of antibodies interfering with such interaction and 8D0 hybridoma cells did not bind to the artificial APC presenting the correct peptide in the context of IEd. The result indicated that highly specific and sensitive interaction occurs between T cells and artificial APCs.

L83 ANSWER 7 OF 41 WPIX (C) 2002 THOMSON DERWENT
AN 2001-408765 [43] WPIX
DNC C2001-123801
TI Component for an adjuvant capable of miscelle formation, for use in a vaccine, comprises a peptide head group and a lipophilic tail group.
DC B04 D16
IN RAMESH, B S; ZUCKERMAN, J N
PA (UNLO) UNIV COLLEGE LONDON
CYC 21

PI WO 2001047553 A1 20010705 (200143)* EN 19p A61K039-39 <--
RW: AT BE CH CY DE DK ES FI FR GB GR IE IT LU MC NL PT SE TR
W: JP US
ADT WO 2001047553 A1 WO 2000-GB4937 20001221
PRAI GB 1999-30591 19991223
IC ICM **A61K039-39**
ICS **A61K009-127**
ICA C07K005-09; C07K007-06
AB WO 200147553 A UPAB: 20010801
NOVELTY - A component (I) for an adjuvant capable of miscelle formation, comprising a peptide head group for binding to an antigen-presenting cell, and a lipophilic tail group.
DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following:
(1) an adjuvant comprising a micelle comprising more than one (I); and
(2) a vaccine composition comprising an antigen and (1).
ACTIVITY - Immunostimulant. No suitable biological data is given.
MECHANISM OF ACTION - Vaccine.
USE - (I) is used in an adjuvant, which is capable of miscelle formation, for a vaccine (claimed).
ADVANTAGE - (I) can be used in an adjuvant which does not produce granulomas at injection sites, unlike Freund's adjuvants. The new adjuvant can bind to specific cells as it has miscelle-forming properties. It can elicit a T-cell mediated immune response. There is no size restriction on particle size.
Dwg.0/0
FS CPI
FA AB; DCN
MC CPI: B04-B01B; **B04-B04C**; B04-C01C; **B04-H20**; B04-N04; B14-G01; B14-S11; D05-H07; D05-H17C
TECH UPTX: 20010801
TECHNOLOGY FOCUS - ORGANIC CHEMISTRY - Preparation: (I) is prepared using standard solid phase synthesis techniques.

TECHNOLOGY FOCUS - BIOTECHNOLOGY - Preferred Component: The head group of (I) comprises a motif for binding to a receptor on the antigen-presenting cell. The motif comprises a sequence of amino acids in the peptide head group, preferably made up of Arg, Gly and Asp. The receptor comprises an integrin. The motif comprises the L amino acid sequence Arg Gly Asp and the lipophilic tail group is the N terminal of Arg. Alternatively, the peptide motif comprises D amino acids and has a sequence of Asp Asp Asp Gly Gly Gly Gly Gly Arg Arg Arg and the lipophilic tail group is the N-terminal of the D amino acid. The lipophilic tail group comprises a C8 - C12 fatty acid. The fatty acid comprises lauric acid.
ABEX
EXAMPLE - No suitable example is given.

L83 ANSWER 8 OF 41 WPIX (C) 2002 THOMSON DERWENT
AN 2001-367316 [38] WPIX
DNC C2001-112592
TI Compositions comprising isolated porcine B7-1 proteins or nucleic acids encoding the proteins, useful for treating and preventing xenograft rejection, autoimmune diseases and inflammatory diseases.
DC A96 B04 D16 D22
IN FAAS KNIGHT, S; FODOR, W L; MATIS, L A; ROTHER, R P
PA (ALEX-N) ALEXION PHARM INC
CYC 92
PI WO 2001030377 A1 20010503 (200138)* EN 51p A61K038-22
RW: AT BE CH CY DE DK ES FI FR GB GR IE IT LU MC NL PT SE
W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CR CU CZ DE DK DM DZ EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ PL PT RO RU SD SE

SG SI SK SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW
AU 2001012234 A 20010508 (200149) A61K038-22
EP 1140146 A1 20011010 (200167) EN A61K038-22
R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT RO SE SI

ADT WO 2001030377 A1 WO 2000-US29155 20001021; AU 2001012234 A AU 2001-12234 20001021; EP 1140146 A1 EP 2000-973762 20001021, WO 2000-US29155 20001021

FDT AU 2001012234 A Based on WO 200130377; EP 1140146 A1 Based on WO 200130377

PRAI US 1999-161140P 19991022

IC ICM A61K038-22
ICS **A61K039-395**; **A61K047-00**; C07H021-04; C07K014-705; C07K016-28; C12N015-63; C12N015-70; C12N015-85

AB WO 200130377 A UPAB: 20010711

NOVELTY - A composition (C) comprising isolated porcine B7-1 proteins (I) having at least 80% sequence identity to a porcine B7-1 protein sequence, or a nucleic acid sequence (II) having at least 80% identity to a molecule encoding (I) including its allelic variants, is new.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following:

(1) a vector (III) comprising a nucleic acid sequence (S1) fully defined in the specification;

(2) a host cell (IV) comprising (III);

(3) an antibody (Ab) which binds to (I);

(4) agents (A) for the diagnosis of porcine xenograft rejection based upon Ab;

(5) porcine cells, tissues or whole organs characterized by the absence of B7-1 molecules; and

(6) a therapeutic agent (V) for the prevention and/or treatment of porcine xenograft rejection or inflammatory disease, comprising (I) or Ab.

ACTIVITY - Immunosuppressive; antiinflammatory.

Short term primary human allogenic and xenogeneic MLRs (mixed lymphocyte reactions) were established and treated with increasing amounts of soluble B7-1 proteins. Cells were maintained for 4-5 days at 37 deg. C in 5% CO2. (3H)thymidine was added to the cell cultures during the last 16-18 hours of incubation. The cells were harvested and subjected to a beta liquid scintillation counter for cell counting. Addition of sB7-1 at high concentrations (25-100 micro g/ml) inhibited both allogeneic- and xenogeneic-stimulated T cell proliferation. Addition of murine CTLA-4Ig at a concentration of 100 micro g/ml effectively inhibited cell proliferation in both assays, while addition of porcine **P-selectin** -His made at Alexion (100 micro g/ml) had no effect on cell proliferation. The results indicated that binding of porcine sB7-1 to CD28 and/or CRLA-4 ligands or human T cells inhibits their activation by allogeneic or xenogeneic stimulation in a concentration-dependent manner.

MECHANISM OF ACTION - Vaccine; gene therapy.

USE - Ab is useful for treating porcine xenograft rejection and inflammatory disease, along with an immunosuppressive agent e.g., cyclosporin A, FK506, rapamycin and a corticosteroid (claimed).

Dwg.0/8

FS CPI

FA AB; DCN

MC CPI: A03-A04A1; A03-C01; A05-E01D; A12-V01; B04-E03F; B04-E05; B04-E08; B04-F0100E; B04-F02; B04-N04; B04-P01B0E; B11-C08E5; B12-K04F; B12-M05; B12-M11E; B14-C03; B14-G02; B14-G02C; **B14-S03**; B14-S11; D05-H07; D05-H11; D05-H12A; D05-H12E; D05-H14A3; D05-H14B2; D05-H16A; D09-C01C

TECH UPTX: 20010711

TECHNOLOGY FOCUS - BIOTECHNOLOGY - Preferred Composition: (C) comprises (II), which is a cDNA comprising (S1). (C) comprises a transmembrane and cytoplasmic domain deleted variant comprising (S2) defined in the specification.

Preferred Cell: (IV) is a CHO cell (Chinese hamster ovary cell), Escherichia coli, yeast, COS cell of L cells, C127 mammary epithelial

cell, Balb/3T3 cell, 293 EBNA, HeLa cell, myeloma, BHK cell, picia or tobacco.
Preferred Agent: (V) further comprises anti-porcine B7-2 antibodies and/or soluble B7-1 molecules.
Preferred Antibody: Ab is a monoclonal, polyclonal, humanized, bispecific, heteroconjugate antibody such as chimeric or CDR grafted antibody, or its fragments. Ab binds to porcine B7-1 proteins but not to human B7-1.

ABEX

WIDER DISCLOSURE - The following are also disclosed as new:
(1) soluble and transmembrane porcine B7-1 proteins (sB7-1 and tmB7-1, respectively), and their amino acid sequences;
(2) nucleic acids encoding sB7-1 and tmB7-1 proteins; and
(3) producing B7-1 proteins or nucleic acids encoding B7-1 proteins.

ADMINISTRATION - (V) is administered through bolus dosage, intravenous injection or by continuous infusion, in the form of microcapsules comprising hydroxymethylcellulose or gelatin, liposomes, or sustained-release matrices e.g., polyesters, hydrogels and injectable microspheres of biodegradable materials (claimed). Dosage ranges from 1-100 mg/kg.

EXAMPLE - Transmembrane form of porcine B7-1 (tmB7-1) was isolated by RT-PCR (reverse transcription polymerase chain reaction) of freshly isolated porcine lung RNA using an oligonucleotide from the 3' end of the sB7-1 coding region as the 5' primer (GCTACCAACACGATGCTTTCC) and oligo dT16 as the 3' primer. The two major products resulting from the RT-PCR were cloned into pCR2.1-TOPO and inserts were sequenced for identification. One of the clones obtained through PCR (tmB7-1) contained the complete transmembrane domain coding region and most of the cytoplasmic domain coding region (based on comparison with B7-1 from other species), but the translational stop site and 3' UTR were not present. The truncation of tmB7-1, and the lack of detection of tmB7-1 in the oligo dT primed porcine macrophage library suggested strong 3' UTR secondary structure in the transcripts.

L83 ANSWER 9 OF 41 WPIX (C) 2002 THOMSON DERWENT
AN 2000-681105 [67] WPIX
DNC C2000-207282
TI Compositions to deliver compounds into cells e.g. to treat rheumatoid arthritis, comprise organic halide, targeting ligand and nuclear localization sequence in combination with compound and **carrier**.
DC A96 B07 D16
IN MCCREERY, T; SADEWASSER, D A; UNGER, E C
PA (IMAR-N) IMARX PHARM CORP
CYC 25
PI EP 1046394 A2 20001025 (200067)* EN 78p A61K009-127 <--
R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT RO SE SI
ADT EP 1046394 A2 EP 2000-303249 20000418
PRAI US 1999-294623 19990419
IC ICM **A61K009-127**
ICS A61K048-00; C12N015-88
AB EP 1046394 A UPAB: 20001223
NOVELTY - Compositions for delivering compounds into cells comprise: an organic halide; a targeting ligand; and a nuclear localization sequence in combination with the compound to be delivered.
ACTIVITY - Immunoregulatory; anti-inflammatory; anti-arthritic.
USE - The compositions are used to deliver compounds into cells (claimed), particularly for the treatment of autoimmune disorders and inflammatory conditions such as rheumatoid arthritis. They may also be used to deliver pharmaceuticals, drugs, diagnostic agents, synthetic organic molecules, peptides, proteins, vitamins, steroids, genetic materials and other bioactive agents e.g. mitotic inhibitors (vinca

alkaloids), radiopharmaceuticals (radioactive iodine, phosphorus and cobalt isotopes), hormones (progestins, estrogens, anti-estrogens), anthelmintics, antimalarials, antituberculotics, biologicals (immune sera, antitoxins, antivenoms), rabies prophylactic products, bacterial vaccines, viral vaccines, aminoglycosides, respiratory products (xanthine derivatives, theophylline, aminophylline), thyroid therapeutics (iodine salts, antithyroid agents), cardiovascular products (chelating agents, mercurial diuretics, cardiac glycosides), glucagons, blood products (parenteral iron, hemin, hematoporphyrins and derivatives), targeting ligands (peptides, antibodies, antibody fragments), biological response modifiers (muramyl dipeptide, muramyl tripeptide, microbial cell wall components, lymphokines - bacterial endotoxin e.g. lipopolysaccharide and macrophage activation factor), subunits of bacteria (Mycobacteria, Comebacteria), synthetic dipeptides (N-acetyl-muramyl-L-alanyl-D-isoglutamine), antifungals (ketoconazole, nystatin, griseofulvin, flucytosine, miconazole, amphotericin B), toxins (ricin), immunosuppressants (cyclosporins), antibiotics (beta -lactam, sulfazecin), hormones (growth hormone, melanocyte-stimulating hormone, estradiol, beclomethasone dipropionate, betamethasone, betamethasone acetate, betamethasone sodium phosphate, betamethasone disodium phosphate, cortisone acetate, dexamethasone, dexamethasone acetate, dexamethasone sodium phosphate, flunisolide, hydrocortisone, hydrocortisone acetate, hydrocortisone cypionate, hydrocortisone sodium phosphate, hydrocortisone sodium succinate, methylprednisolone, methylprednisolone acetate, methylprednisolone sodium succinate, paramethasone acetate, prednisolone acetate, prednisolone sodium phosphate, prednisolone tebutate, prednisone, triamcinolone, triamcinolone acetonide, triamcinolone diacetate, triamcinolone hexacetonide, fluorocortisone acetate, oxytocin, vasopressin and their derivatives), vitamins (cyanocobalamin neionic acid), retinoids and their derivatives (retinal palmitate, alpha -tocopheryl), peptides and enzymes (manganese superoxide dismutase, alkaline phosphatases), anti-allergens (amelexanox), anticoagulants (phenprocoumon, heparin), tissue plasminogen activators, streptokinase and urokinase), circulatory drugs (propranolol), metabolic potentiators (glutathione), antibiotics (p-aminosalicylic acid, isoniazid, capreomycin sulfate, cycloserine, ethambutol hydrochloride, ethionamide, pyrazinamide, rifampicin, streptomycin sulfate dapsone, chloramphenicol, neomycin, ceflacor, cefadroxil, cephalexin, cephadrine erythromycin, clindamycin, lincomycin, amoxicillin, ampicillin, bacampicillin, carbenicillin, dicloxicillin, cyclacillin, picloxicillin, hetacillin, methicillin, nafcillin, oxacillin, penicillin (G and V), ticarcillin, rifampin, tetracycline), antivirals (acyclovir, ddI, foscarnet, zidovudine, ribavirin, vidarabine monohydrate), antianginals (diltiazem, nifedipine, verapamil, erythritol tetranitrate, isosorbide dinitrate, nitroglycerin (glyceryl trinitrate), pentaerythritol tetranitrate, anti-inflammatories (difluisal, ibuprofen, indomethacin, meclofenamate, mefenamic acid, naproxen, oxyphenbutazone, phenylbutazone, piroxicam, sulindac, tolmetin, aspirin, salicylates), antiprotozoans (chloraquine, hydroxychloraquine, metronidazole, quinine, meglumine antimonate), antirheumatics (penicillamine), narcotics (paregoric), opiates (codeine, heroin, methadone, morphine, opium), cardiac glycosides (deslanoside, digitoxin, digoxin, digitalin, digitalis), neuromuscular blockers (atracurium mesylate, gallamine triethiodide, hexafluorenium bromide, metrocurine iodide, pancurium bromide, succinylcholine chloride (suxamethionium chloride), tubocurarine chloride, vencuronium bromide), sedatives (amobarbital, amobarbital sodium, aprobarbital, butabarbital sodium, chloral hydrate, ethchlorvynol, ethinamate, flurazepam hydrochloride, glutethimide, methotrimeprazine hydrochloride, methyprylon, midazolam hydrochloride, paraldehyde, pentobarbital, pentobarbital sodium, secobarbital sodium, thiopental sodium), antineoplastics (methotrexate, fluorouracil, adriamycin, mitomycin, ansamitomycin, bleomycin, cysteine arabinoside, arabinosyl adenine, mercaptopolylysine, vincristine, busulfan, chlorambucil, azidothymidine, melphalan (e.g. PAM, L-PAM or phenylalanine mustard),

mercaptopurine, mitotane, procarbazine hydrochloride, dactinomycin (actinomycin D), daunorubicin hydrochloride, dosorubicin hydrochloride, Taxol (RTM: paclitaxel), plicamycin (mithramycin), aminoglutethimide, estramustine phosphate sodium, flutamide, leuprolide acetate, megestrol acetate, tamoxifen citrate, testolactone, trilostane, amsacrine (m-AMSA), asparaginase, etoposide (VP-16), interferon alpha -2a, interferon alpha -2b, teniposide (VM-26), vinblastine sulfate (VLB), vincristine sulfate, hydroxyurea, procarbaxine or dacarbazine).

ADVANTAGE - The compositions provide improved delivery of compositions including drugs and genetic materials into cells. They provide for specific targeting and delivery of compounds to particular cells and increased targeting to the nuclei of targeted cells. They also allow delivery to cell lines that would be otherwise resistant to intracellular delivery and gene expression using other conventional means.

DESCRIPTION OF DRAWING(S) - Schematic representation of a targeted composition.

targeted composition 1
lipid coating 2
lipids 2A
halocarbon gas or liquid 3
genetic material 4
targeting ligand 5
lipid head group 6
tether 7
tether 7A
nuclear localization sequence 8
condensing agent. 9

Dwg.2/2

FS CPI

FA AB; GI; DCN

MC CPI: A12-V01; B04-B04D; B04-E02D; B04-E06; B04-E07; **B04-G01**; B04-H01; B04-J01; B04-K01V; B14-A01; B14-A02; B14-A03; B14-A04; B14-B03; B14-C03; B14-C09B; B14-F01; B14-G02A; B14-G02D; B14-L01; B14-S11; D05-C10; D05-C12; D05-H12B; D05-H12D2; D05-H12D4; D05-H12D5

TECH UPTX: 20001223

TECHNOLOGY FOCUS - ORGANIC CHEMISTRY - Preferred organic halide - The organic halide is a gaseous or liquid organic halide, preferably a liquid or a gaseous precursor. The organic halide is a fluorinated compound, preferably a perfluorinated compound, more preferably a perfluorocarbon, especially a perfluoroether compound. The organic halide is 1-bromo-nonafluorobutane, perfluorooctyliodide, perfluorooctylbromide, 1-chloro-1-fluoro-1-bromomethane, 1,1,1-trichloro-2,2,2-trifluoroethane, 1,2-dichloro-2,2-difluoroethane, 1,1-dichloro-1,2-difluoroethane, 1,2-dichloro-1,1,3-trifluoropropane, 1-bromoperfluorobutane, 1-bromo-2,4-difluorobenzene, 2-iodo-1,1,1-trifluoroethane, 5-bromovalerylchloride, 1,3-dichlorotetrafluoroacetone, bromine pentafluoride, 1-bromo-1,1,2,3,3,3-hexafluoropropane, 2-chloro-1,1,1,4,4,4-hexafluoro-2-butene, 2-chloropentafluoro-1,3-butadiene, iodotrifluoroethylene, 1,1,2-trifluoro-2-chloroethane, 1,2-difluorochloroethane, 1,1-difluoro-2-chloroethane, 1,1-dichlorodifluoromethane, dibromofluoromethane, chloropentafluoroethane, bromochlorodifluoromethane, dichloro-1,1,2,2-tetrafluoroethane, 1,1,1,3,3-pentafluoropentane, perfluorotributylamine, perfluorotripropylamine, 3-fluorobenzaldehyde, 2-fluoro-5-nitrotoluene, 3-fluorostyrene, 3,5-difluoroaniline, 2,2,2-trifluoroethylacrylate, 3-(trifluoromethoxy)-acetophenone, 1,2,2,3,3,4,4-octafluorobutane, 1,1,1,3,3-pentafluorobutane, 1-fluorobutane, 1,1,2,2,3,3,4,4-octafluorobutane, 1,1,1,3,3-pentafluorobutane, perfluoro-4-methylquinolizidine, perfluoro-N-methyl-decahydroquinone, perfluoro-N-methyl-decahydroisoquinone, perfluoro-N-cyclohexyl-pyrrolidine, perfluoroheptane, perfluorocyclohexane, perfluoromethane (preferred), perfluoroethane (preferred), perfluoropropane (preferred), perfluorobutane (preferred), perfluoropentane (preferred), perfluorohexane

(preferred), perfluoroheptane (preferred), perfluorooctane (preferred), perfluorononane (preferred), perfluorodecane (preferred), perfluorododecane (preferred), perfluoro-2-methyl-2-pentene (preferred), perfluorocyclohexane (preferred), perfluorodecalin (preferred), perfluorododecalin (preferred), perfluoropropylene, perfluorocyclobutane, perfluoro-2-butyne, perfluoro-2-butene, perfluorobuta-1,3-diene, perfluorobutylethyl ether (preferred), bis(perfluoroisopropyl)ether (preferred), bis(perfluoropropyl)ether (preferred), perfluorotetrahydropyran (preferred), perfluoromethyl tetrahydrofuran (preferred), perfluoro-tertiary butyl-methyl ether (preferred), perfluoro-isobutyl-methyl ether (preferred), perfluoro-n-butyl-methyl ether, perfluoro-isopropyl-methyl ether (preferred), perfluoro-n-propyl-methyl ether (preferred), perfluorodiethyl ether (preferred), perfluorocyclopropyl methyl ether (preferred), perfluoromethyl ethyl ether (preferred), perfluorodimethyl ether (preferred), sulfur hexafluoride or selenium hexafluoride.

TECHNOLOGY FOCUS - BIOTECHNOLOGY - Preferred compositions - The compositions further comprises a **carrier** such as a polymer, lipid, protein or metal ion. The **carrier** preferably comprises a lipid, more preferably a cationic lipid, especially N-(1-(2,3-dioleoyloxy)propyl)-N,N,N-trimethylammonium chloride. The **carrier** preferably comprises a polymer, more preferably a polyethylene, polyoxyethylene, polypropylene, pluronic acid or alcohol, polyvinyl, polyvinylpyrrolidone, arabinan, fructan, fucan, galactan, galacturonan, glucan, mannan, xylan, levan, fucoidan, carrageenan, galactocarolose, pectin, pectic acid, amylose, pullulan, glycogen, amylopectin, cellulose, carboxylmethylcellulose, hydroxypropylmethylcellulose, dextran, pustulan, chitin, agarose, keratan, chondroitin, dermatan, hyaluronic acid, alginic acid, homopolymer or heteropolymer containing one or more of an aldose, ketose, acid, amine, erythrose, threose, ribose, arabinose, xylose, lyxose, allose, altrose, glucose, mannose, gulose, idose, galactose, talose, erythrulose, ribulose, xylulose, psicose, fructose, sorbose, tagatose, glucuronic acid, gluconic acid, glucaric acid, galacturonic acid, mannuronic acid, guluronic acid, glucosamine, galactosamine or neuraminic acid. The **carrier** is Lipofectin, Lipofectamine, Transfectace, Transfectam, Cytofectin, dimyristoyloxypropyl-3-dimethylhydroxyethylammonium bromide (DMRIE), dilauryloxypropyl-3-dimethylhydroxyethylammonium bromide (DLRIE), GAP-DLRIE, 1,2-dioleoyloxy-3-(trimethylammonio)propane (DOTAP), dioleoylphosphatidylethanolamine (DOPE), DMEAP, DODMP, dioleoylphosphtadiylcholine (DOPC), DDAB, 2,3-dioleoyloxy-N-(2-(sperminecarboxamidoethyl)-N,N-dimethyl-1-propanaminium trifluoroacetate (DOSPA), EDLPC, EDMPC, DPH, TMADPH, cetyltrimethylammonium bromide (CTAB), lysyl-PE, 3,beta-(N,(N',N'-dimethylaminoethane)carbamoyl)cholesterol (DC-Chol), alanyl cholesterol, DCGS, dipalmitoylphosphatidylethanolamine-5-carboxyspermylamide (DPPES), dicaproylphosphatidylethanolamine (DC PE), 4-dimethylaminopyridine (DMAP), dimyristoylphosphatidylethanolamine (DMPE), dioctadecylamidoglycol spermidine (DOGS), DOFIME, dipalmiotylethylphosphatidylcholine (DPEPC), Pluronic (RTM: polyethylene glycol), Tween (RTM: polysorbate), Brij (RTM: polyoxyethylene glycol), plasmalogen, phosphatidylethanolamine, phosphatidylcholine, glycerol-3-ethylphosphatidylcholine, dimethylammonium propane, trimethylammonium propane, dimethyldioctadecylammonium bromide, sphingolipids, sphingomyelin, lysolipid, glycolipid, sulfatide, glycosphingolipid, cholesterol, cholesterol ester, cholesterol salt, oil, 1,2-dioleoyl-sn-glycerol, N-succinyldioleoylphosphatidylethanolamine, 1,3-dipalmitoyl-2-succinyl-glycerol, 1,2-dipalmitoyl-sn-3-succinylglycerol, palmitoylhomocysteine, 1-hexadecyl-2-palmitoylglycerophosphatidylethanolamine, N,N''-bis(dodecylaminocarbonylmethylene)-N,N'-bis((N,N,N-trimethylammoniumethylaminocarbonylethylene)ethylene diamine tetraiodide, N,N''-bis(hexad ecylaminocarbonylmethylene)-N,N,N''-tris-N,N,N-trimethylammoniumethylaminocarbonylmethylenediethylenetriamine hexaiodide,

N,N'-bis(dodecylaminocarbonylmethylene)-N,N''-bis((N,N,N-trimethylammoniumethylaminocarbonyl-methylene)-cyclohexylene-1,4-diamine-tetraiodide, 1,1,7,7-tetra((N,N,N-tetramethylammoniumethylaminocarbonylmethylene)-3-hexadecylaminocarbonylmethylene-1,3,7-triaazaheptane heptaiodide or N,N,N',N'-tetra-((N,N,N-trimethylammoniumethylaminocarbonylmethylene)-N'-(1,2-dioleoylglycero-3-phosphoethanolaminocarbonylmethylene) diethylene triamine tetraiodide. The **carrier** comprises a dioleoylphosphatidylethanolamine, fatty acid, lysolipid, phosphatidylcholine, phosphatidylethanolamine, phosphatidylserine, phosphatidylglycerol, phosphatidylinositol, sphingolipid, glycolipid, glucolipid, sulfatide, glycosphingolipid, phosphatidic acid, palmitic acid, stearic acid, arachidonic acid, oleic acid, lipid bearing a polymer, lipid bearing a sulfonated saccharide, cholesterol, tocopherol hemisuccinate, lipid with an ether-linked fatty acid, lipid with an ester-linked fatty acid, polymerized lipid, diacetyl phosphate, stearylamine, cardiolipin, phospholipid with a fatty acid of 6-8C, phospholipid with asymmetric acyl chains, 6-(5-cholesten-3b-yloxy)-1-thio-b-D-galactopyranoside, digalactosyldiglyceride, 6-(5-cholesten-3beta-yloxy)hexyl-6-amino-6-deoxy-1-thio-b-D-galactopyranoside, 6-(5-cholesten-3b)-yloxy)hexyl-6-amino-6-deoxyl-1-thio-alpha-D-mannopyranoside, 12-(((7'-diethylamino-coumarin-3-yl)carbonyl)methylamino)octadecanoic acid, N-(12-(((7'-diethylamino-coumarin-3-yl)carbonyl)methylamino)octadecanoyl)-2-aminopalmitic acid, cholesteryl (4'-trimethyl-ammonio)butanoate, N-succinyldioleoylphosphatidylethanolamine, 1,2-dioleoyl-sn-glycerol, 1,2-dipalmitoyl-sn-3-succinyl-glycerol, 1,3-dipalmitoyl-2-succinylglycerol, 1-hexadecyl-2-palmitoylglycerophosphoethanolamine and/or palmitoylhomocysteine. The **carrier** comprises a phosphatidylcholine, preferably dioleoylphosphatidylcholi ne, dimyristoylphosphatidylcholine, dipentadecanoylphosphatidylcholine, dilauroylphosphatidylcholine, dipalmitoylphosphatidylcholine or distearoylphosphatidylcholine. The **carrier** comprises phosphatidylethanolamine, preferably dioleoylphosphatidylethanolamine. The **carrier** comprises a glycolipid, preferably ganglioside GM1 or GM2. The **carrier** comprises a lipid bearing a polymer, preferably polyethylene glycol, chitin, hyaluronic acid or polyvinylpyrrolidone, more preferably polyethylene glycol, especially a polyethylene glycol with a molecular weight of 2,000, 5,000 or 8,000. The **carrier** comprises a phospholipid with asymmetric acyl chains with one acyl chain of about 6 C in length and another of about 12 C in length. The **carrier** comprises about 82 mole % dipalmitoylphosphatidylcholine, about 8 mole % dipalmitoylphosphatidylethanolamine-polyethylene glycol 5,000 and about 10 mole % dipalmitoylphosphatidic acid. The **carrier** comprises a surfactant, preferably a fluorosurfactant. The compositions further comprise a telomerase. The compositions further comprise a fusion peptide.

Preferred delivery compound - The compound to be delivered is a pharmaceutical agent, synthetic organic molecule, protein, peptide or genetic material, preferably a mutant gene that encodes a defective receptor chosen from tumor necrosis factor (TNF), gamma interferon (IFN gamma) or interleukin-1 (IL-1), antisense oligonucleotide (that preferably hybridizes to a nucleic acid molecule encoding a protein selected from TNF receptor, IFN gamma receptor or IL-1 receptor) or a ribozyme (a ribozyme that disrupts nucleic acid molecules encoding a protein chosen from TNF receptor, IFN gamma receptor or IL-1 receptor).

Preferred targeting ligand - The targeting ligand is a protein, antibody (fragment), hormone (analog), glycoprotein, lectin, (poly)peptide, amino acid, sugar, saccharide, carbohydrate, vitamin, steroid (analog), cofactor, bioactive agent or genetic material, preferably Sialyl Lewis X (preferred), mucin, hyaluronic acid, LFA-1, VLA-4, fibrinogen, von Willebrand factor, vitronectin, **VCAM-1**, CD49d/CD29, methyl-alpha-D-mannopyranoside, N-formal peptide, C5a, leukotriene B4, platelet-activating factor, IL-8/NAP-1, CTAP-III, beta-thromboglobulin, NAP-2, gro/MGSA, ENA-78, MCP-1, MAP-1alpha,beta, RANTES or I-309.

Preferred nuclear localization sequence - The nuclear localization sequence is a peptide, protein, receptor, transcription factor or an enzyme, especially influenza virus nucleoprotein, karyophenin beta1, human stat1 gene, m-importin, mouse homolog of nuclear pore targeting complex, hepatitis B virus (HBV) polymerase, glucocorticoids receptor (GlucR), interferon-regulated factors ISGF-3 and GAF, yeast mating switch/HO endonuclease promoter SW15, Drosophila melanogaster morphogen dorsal, nuclear factors NF-kappa and NF-AT, T-ag, c-rel, lamin B2, GrH receptor, c-fos, cofilin, rNFIL-6, NF-ATplc, PICA C-subunit, p42mapk/p44erk1, p90rsk, PKC-alpha, lodestar, v-jun, cyclin B (B-type cyclins), adenovirus 5 E1a protein, xnf7, PwA33, Rb-1, p53, c-myc, PTF1, HMG1/2 and tegument protein pp65 (UL83) of human cytomegalovirus. The nuclear localization sequence is a peptide comprising a defined amino acid sequence.

ABEX

SPECIFIC SEQUENCES - A total of 24 nuclear localization sequences are claimed and all are given in the specification. E.g. Pro-Lys-Lys-Lys-Arg-Lys-Val and Asn-Lys-Ile-Pro-Ile-Lys-Asp.

ADMINISTRATION - Administration may be in combination with ultrasound to the cells (claimed).

L83 ANSWER 10 OF 41 WPIX (C) 2002 THOMSON DERWENT
AN 2000-679647 [66] WPIX
DNC C2000-206773
TI New neuromodulator molecule comprising one component to suppress or neutralize neurite growth inhibitory effect of target, and second component capable of stimulating neurite growth and/or regeneration.
DC B04 D16
IN FRAIDAKIS, M; OLSON, L
PA (KARO-N) KAROLINSKA INNOVATIONS AB; (FRAI-I) FRAIDAKIS M
CYC 93
PI WO 2000064482 A1 20001102 (200066)* EN 65p A61K047-48 <--
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW NL OA PT SD SE SL SZ TZ UG ZW
W: AE AG AL AM AT AU AZ BA BB BG BR BY CA CH CN CR CU CZ DE DK DM DZ EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW
AU 2000046343 A 20001110 (200109) A61K047-48 <--
EP 1210120 A1 20020605 (200238) EN A61K047-48 <--
R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT RO SE SI
ADT WO 2000064482 A1 WO 2000-SE764 20000420; AU 2000046343 A AU 2000-46343 20000420; EP 1210120 A1 EP 2000-928054 20000420, WO 2000-SE764 20000420
FDT AU 2000046343 A Based on WO 200064482; EP 1210120 A1 Based on WO 200064482
PRAI SE 1999-1428 19990421
IC ICM **A61K047-48**
ICS A61K038-18; **A61K039-395**
AB WO 200064482 A UPAB: 20001219
NOVELTY - A neuromodulator molecule (I) (an amphibody) comprising two components, in which the first component (C1) is capable of binding to and suppressing or neutralizing a neurite growth inhibitory effect of the target, and a second component (C2) capable of stimulating neurite growth and/or regeneration, is new.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following:

(1) producing (I) by recombinant DNA techniques involves fusing nucleic acids encoding suitable (C1) and (C2) into a recombinant vector, inserting the vector into a suitable host cell and expressing the desired regulator. Alternately, (I) is produced by chemical fusion of (C1) and (C2) with a suitable reagent to produce the desired amphibody;

(2) a vector (II) comprising nucleic acids encoding (I);

(3) a cell (III) comprising (II); and

(4) a pharmaceutical preparation comprising (III) and preferably comprising a suspension of such cells, together with **carrier**, which is suitable for use in gene therapy.

ACTIVITY - Vulnerary; cerebroprotective; neuroprotective; immunosuppressive; antitumor; ophthalmological. No supporting data is given.

MECHANISM OF ACTION - Enhances the growth and regeneration of neurons and nerve fibers; gene therapy.

USE - (I) is useful for producing a medicament for treating and/or preventing spinal cord injury, brain trauma, stroke, retinal and optic nerve lesions, neurodegenerative diseases, neuromuscular diseases, autoimmune diseases of the nervous system, tumors of the central nervous system etc (claimed). The amphibodies, force a non-permissive, or outgrowth-suppressive or chemorepulsive, i.e. an unfavorable environment, encompassing cellular surfaces, extra cellular matrix, molecules in the extracellular fluid, into a permissive, and outgrowth promotive and chemoattractive one. Different amphibodies to be used to peripheral nerve injuries, optic nerve injuries and spinal cord injuries.

ADVANTAGE - (I) provides a specific and localized simultaneous inhibitory and stimulatory action, which cannot be obtained by the administration of two components as such. The amphibodies achieve the vital turnabout change of milieu by, on the spot neutralizing negative cues and in situ exposing positive modulators of axonal growth in a sugarcoat fashion. The amphibodies are more powerful agents since they will not only nullify a multitude of inhibitory factors, but they simultaneously supplement axonotrophic/tropic elements in the region precisely on the spot of previously exposed inhibitory sites, turning a negative environment into a positive one rather than a neutral one.

DESCRIPTION OF DRAWING(S) - The figure shows the principle of the new neuromodulator or modulator amphibody.

Dwg.1/5

FS CPI

FA AB; GI; DCN

MC CPI: B04-E08; B04-F0100E; B04-H01; **B04-H20**; B14-F02D1; B14-G02D; **B14-H01**; B14-J01; **B14-N03**; B14-N16; D05-C12; D05-H12C; D05-H12E; D05-H14; D05-H17C

TECH UPTX: 20001219

TECHNOLOGY FOCUS - BIOTECHNOLOGY - Preferred Neuromodulator: The two components in (I) are separated from each other by a linker element to assume a functional confirmation. (C1) is capable of binding to a target which is a glial cell, a neuron, a fibroblast, a blood cell or an extracellular matrix component, which provides an neurite growth inhibitory effect by expressing a specific neurite growth inhibitory molecule such as NOGO (previously NI-35/250), a myelin associated glycoprotein (MAG), a proteoglycan, a Sem receptor or a member of any one of the families of semaphorins, tenascins, netrins and Eph and ephrins. Preferably, (C1) is IN-1 and the inhibitory factor is NOGO. (C2) is a neurotrophic molecule such as a **cell adhesion molecule** (CAM) e.g. immunoglobulin superfamily CAM, cadherin, integrin or its functional fragment. Preferably, the neurotrophic molecule is an extracellular matrix molecule (ECM). Alternately, the neurotrophic molecule is a member of neurotrophic family, the glial cell derived neurotrophic factor (GDNF)-subfamily, neuropoietic cytokines, fibroblast growth factors (FGF) or hepatocyte growth factor (HGF). The second component is preferably neurotropin (NT)-3 or another neurotrophin such as brain-derived neurotrophic factor (BDNF), nerve growth factor (NGF) or NT-4, or L1.

Preferred Method: Preparation of (I) by chemical fusion involves use of components such as proteins, polypeptides, peptides or carbohydrates. The ratio between (C1) and (C2) during fusion is 1:1. The method further involves a purification step.

ABEX

WIDER DISCLOSURE - Nucleic acids encoding (I) are also disclosed.

ADMINISTRATION - Administration is through intravenous, intraparenchymal, oral, intraventricular, intrathecal routes or by direct gene delivery. No specific clinical dosages are given.

EXAMPLE - The fusion protein consisting of neurotropin (NT)-3 and an Fab version of an antibody to NOGO have the following outline. N-terminal-NT-3-linker-antibody heavy chain (Fd fragment)-stop-antibody light chain. Cloned NT-3 and a cloned Fab antibody, IN-1, (a monoclonal neutralizing antibody to NOGO), were obtained. They were combined using a sequence of point mutations and polymerase chain reaction (PCR) amplifications. The existing stop codon in NT-3 was mutagenized using hybridizing primer (881-s and 848-AS as given in the specification). Nucleic sequencing (with primers 774-S and 169 AS as given in the specification) was performed on the 5' end of the NT-3 cDNA, in order to be able to design PCR primers correctly. The Fd chain of IN-1 was amplified in a two step PCR, in order to extend the 5' end of the resulting product, so that it contained several restriction endonuclease sites, allowing the later insertion of NT-3 5' of the Fd cDNA, as well as a linker region between the insertion site for NT-3 and the antibody chain cDNA. The sequence of IN-1 was located in Genbank. In the first PCR experiment, the primers AB-239-S and AB-912-AS (5' and 3', respectively) were used. In the second PCR, utilizing a fraction of the PCR product from the first reactions template, the primers AB-176-S and AB-912-AS were used. Primer AB-239-S carries a XhoI restriction site, and the second 5' primer AB-176-S carries HindIII, SalI, AgeI sites. The light chain of IN-1 was PCR amplified using primers AB-996-S and AB-1647-AS. Two final PCR products were obtained. The ends were digested with HindIII and NheI (the Fd PCR product and Ecl136II+XbaI(light chain (LC)). They were gel purified in agarose gel. The vector pcHCLC was prepared for subsequent ligation of the Fd and LC PCR products by digestion with HindIII+ NheI, and Hpal+XbaI, for the insertion of Fd and LC PCR products, respectively. The linearized vector DNA was obtained by gel purification. The digested LC PCR product was ligated into pcHCLC. NT-3 cDNA was PCR amplified from the mutagenized version obtained in step 1 using primers 96-S and 848-AS. The PCR product was digested with XhoI and AgeI, and gel purified. The FdPCR product is ligated into pcHCLC already containing the IN light chain DNA followed by digestion with SalI and AgeI and subsequent gel purification of the plasmid obtained above. The digested PCR product obtained, was ligated into the linearized plasmid DNA obtained as described above. The plasmid so obtained was used to transfect mammalian cells and an assay for expression of the recombinant protein is performed. Thus, cells expressing the novel fusion protein were obtained.

L83 ANSWER 11 OF 41 WPIX (C) 2002 THOMSON DERWENT
AN 2000-665196 [64] WPIX
DNN N2000-492972 DNC C2000-201561
TI Increasing the half-life of viral-specific ligands on an animal's mucosal membrane, used to prevent viral infections.
DC B04 B07 D16 P32
IN LEE, P P
PA (OSEL-N) OSEL INC
CYC 93
PI WO 2000062758 A1 20001026 (200064)* EN 40p A61K009-00 <--
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW NL OA PT SD SE SL SZ TZ UG ZW
W: AE AG AL AM AT AU AZ BA BB BG BR BY CA CH CN CR CU CZ DE DK DM DZ EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW
AU 2000043504 A 20001102 (200107) A61K009-00 <--
EP 1171098 A1 20020116 (200207) EN A61K009-00 <--
R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT

RO SE SI
US 6365156 B1 20020402 (200226) A61K039-40 <--
US 2002086020 A1 20020704 (200247) A61K039-42 <--
ADT WO 2000062758 A1 WO 2000-US10079 20000414; AU 2000043504 A AU 2000-43504 20000414; EP 1171098 A1 EP 2000-923364 20000414, WO 2000-US10079 20000414; US 6365156 B1 Provisional US 1999-129722P 19990416, US 2000-549261 20000414; US 2002086020 A1 Provisional US 1999-129722P 19990416, Div ex US 2000-549261 20000414, US 2002-43689 20020110
FDT AU 2000043504 A Based on WO 200062758; EP 1171098 A1 Based on WO 200062758
PRAI US 1999-129722P 19990416; US 2000-549261 20000414; US 2002-43689 20020110
IC ICM **A61K009-00**; **A61K039-40**; **A61K039-42**
ICS A61F006-06; A61F013-00; **A61K009-20**; **A61K009-48**; **A61K039-385**; **A61K039-395**; C07K001-00; C07K014-00; C07K017-00
AB WO 200062758 A UPAB: 20001209
NOVELTY - Increasing the half-life of a viral-specific ligand on an animal's mucosal membrane, which is colonized with bacteria, comprising contacting the membrane with a viral-specific ligand modified to bind to the surface of the colonizing bacteria, is new.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following:

(1) a chimeric molecule, comprising a viral-specific ligand and a bacterial-specific ligand , where the bacterial-specific ligand binds to a bacteria that inhabits the mucosal membrane;

(2) manufacturing a chimeric molecule, comprising joining a viral-specific ligand to a bacterial-specific ligand, where the bacterial-specific ligand binds to bacteria inhabiting the mucosal membrane and the viral-specific ligand binds to infectious viral particles;

(3) binding viral particles to bacteria inhabiting the mucosal membrane of an animal, comprising contacting the bacteria with a viral-specific ligand having a bacterial-specific ligand, and permitting viral particles specifically recognized by the ligand to bind to the bacteria;

(4) a system for delivering a unit dose of a chimeric molecule to nasal mucosa in a physiologically compatible solution, comprising:

(a) a chimeric molecule in a sterile solution, the molecule comprising a viral-specific ligand able to bind viral particles and a bacterial-specific ligand which binds to bacteria that naturally inhabits a healthy mucosal membrane; and

(b) a container having a base end containing the solution, and a tapered tip end having an opening for delivering a metered and aerosol spray of the solution into a nasal passage; and

(5) a pharmaceutical composition comprising a chimeric molecule or a viral-specific ligand modified by binding a bacterial-specific ligand.

ACTIVITY - Antiviral. No biological data is given.

MECHANISM OF ACTION - Viral-specific ligand.

USE - For improving the half-life of soluble viral-specific ligands on the mucosal membrane (claimed), used to prevent viral infections.

ADVANTAGE - The improved half-life of the soluble viral-specific ligands on the mucosal membrane reduces the cost and application frequency associated with the use of viral-specific ligands to prevent viral infections.

Dwg.0/2
FS CPI GMPI
FA AB; DCN
MC CPI: B04-N04; B11-C04; B12-M01A; B14-A02; D05-H17C
TECH UPTX: 20001209
TECHNOLOGY FOCUS - BIOTECHNOLOGY - Preferred Method: The viral-specific ligand is modified to bind to bacteria colonizing the mucosal membrane, preferably Lactobacillus, Streptococcus, Staphylococcus, Lactococcus, Bacteroides, Bacillus or Neisseria. Alternatively, the ligand is modified

by binding to a bacterial- or viral-specific ligand, preferably an antibody, such as a single chain antibody, a F(ab) or a F(ab)2, or a peptide, polypeptide, and/or carbohydrate. Alternatively, the bacterial-specific ligand is a C-terminal choline binding domain of LytA or PspA, a C-terminal domain of lysostaphin (SPACWT), a C-terminal domain of InIB, an anti-S-layer protein antibody, or an anti-peptidoglycan antibody. The binding of the two ligands uses a bifunctional linking reagent, a covalent bond or a peptide linker. The viral specific ligand is CD4, DC-SIGN, inter-**cellular adhesion molecule** (**ICAM**)-**1**, HveA, HveC, poliovirus receptor, vitronectin receptor, CD21 or immunoglobulin (Ig)A receptor sequences, or a carbohydrate, preferably sialic acid or heparin sulfate.
Preferred Molecule: The chimeric molecule is in a sterile aqueous solution, especially a physiologically compatible solution.
Preferred System: The base is flexible and allows the transfer of pressure from the container to the solution, allowing the fluid to be emitted from the tapered end.
Preferred Composition: The composition is a solution, a powder, a cream, a gel, an ointment, a douche, a suspension, a tablet, a pill, a capsule, a nasal spray, a nasal drop, a suppository, an aerosol, a pessary, a tampon, a paste, a foam or a spray.

ABEX

EXAMPLE - The polypeptide comprising inter-cellular adhesion molecule (ICAM)-1 domains 1 and 2 (the receptor for human rhinovirus (HRV)) was expressed as a fusion protein with the C-terminal domain of lysostaphin, SPACWT, to target the chimeric molecule to the surface of Staphylococcus aureus. The DNA fragments coding for domains 1 and 2 of ICAM-1 and SPACWT were amplified using polymerase chain reaction with primers designed to introduce in-frame EcoRI restriction sites flanking residues 1-168 of ICAM-1 and residues 389-480 of lysostaphin (SPACWT). These fragments were ligated together and placed into a mammalian expression cassette for expression in mammalian cell lines, the cassette contains the selectable marker Herpes thymidine kinase (TK). Chimeric molecules were expressed in Chinese hamster ovary (CHO) cells. The expression vector containing the DNA fragments coding for ICAM-1 domains 1 and 2 and SPACWT was transfected into CHO cells under standard conditions. These cells were grown up in large numbers in standard culture medium (Dulbecco's modified essential medium containing 10 % fetal bovine serum), transfectants were selected by the addition of HAT (hypoxanthine/aminoptherin/thymidine) to the medium to maintain selective pressure for the marker Herpes TK. After a growth period of 48-96 hours, cells were lysed to release the cytosolic contents containing the chimeric molecules. Cells were solubilized for 1 hour at 4 degrees C in a physiologic buffer containing the non-ionic detergent Triton-X-100 and a cocktail of protease inhibitors (aprotinin and leupeptin at 10 micro-g/ml, ethylenediaminetetraacetic acid (EDTA) at 1 mM) to prevent proteolytic degradation of the molecules. The chimeric molecules were purified using monoclonal antibody affinity chromatography. The monoclonal antibody RR1/1 which reacts with ICAM-1, is coupled to an inert column matrix. The cell lysate from CHO cells containing chimeric molecules is passed through precolumns to remove materials that bind non-specifically to the column matrix material, then through the RR1/1-immobilized column. The ICAM-1 moiety of the chimeric molecule bonded to the antibody and was immobilized on the column. The column was washed extensively with a series of detergent wash buffers of increasing pH, upto pH 11.0. During these washes, chimeric molecules remain bound to the column, while non-binding and weakly binding contaminants were removed. The bound chimeric molecules were then specifically eluted from the column by applying a detergent buffer of pH 12.5.

L83 ANSWER 12 OF 41 WPIX (C) 2002 THOMSON DERWENT
AN 2000-491015 [43] WPIX
DNC C2000-147560
TI Solid microspheres for immunization of mammals to achieve cell-mediated

and humoral immune responses, comprising encapsulated cytokine.

DC B04 D16

IN AUGUST, J T; LEONG, K W; LIU, S Q; SONG, R

PA (UYJO) UNIV JOHNS HOPKINS SCHOOL MEDICINE

CYC 21

PI WO 2000041679 A1 20000720 (200043)* EN 34p A61K009-16 <--
RW: AT BE CH CY DE DK ES FI FR GB GR IE IT LU MC NL PT SE
W: JP US
EP 1143934 A1 20011017 (200169) EN A61K009-16 <--
R: AT BE CH CY DE DK ES FI FR GB GR IE IT LI LU MC NL PT SE

ADT WO 2000041679 A1 WO 2000-US730 20000113; EP 1143934 A1 EP 2000-901411 20000113, WO 2000-US730 20000113

FDT EP 1143934 A1 Based on WO 200041679

PRAI US 1999-116242P 19990115; US 1999-115849P 19990113

IC ICM **A61K009-16**
ICS **A61K009-51**; A61K038-19; **A61K039-39**

AB WO 200041679 A UPAB: 20000907
NOVELTY - Solid microsphere (I) encapsulating a cytokine, but not comprising DNA for use in the genetic immunization of a mammal, is new.

DETAILED DESCRIPTION - An INDEPENDENT CLAIM is also included for a method (II) of forming solid microspheres by coacervation of a polyanion (not a nucleic acid) and a polymeric cation (comprising chitosan or gelatin) in the presence of a cytokine which is encapsulated.

ACTIVITY - Antiviral; anti-HIV.

MECHANISM OF ACTION - Vaccine.

The effect of microsphere-encapsulated, IL-2 and gamma -INF on cytotoxic T lymphocyte (CTL) response was evaluated.

Mice were immunized with a single injection of microspheres containing p43-clacZ DNA (cytomegalovirus-intron A-lacZ) alone, with IL-2 or with IL-2 and gamma -INF and examined for the generation of anti- beta -gal cytotoxic T lymphocyte (CTL) response at week 4. The results showed that mice vaccinated with microsphere alone or naked DNA generated a poor CTL response. When IL-2 was included in the microsphere an enhancement in CTL response was observed. The inclusion of both IL-2 and gamma -INF in the microsphere improved anti- beta -gal CTL response from 25 % lysis to 65 % with a single immunization.

USE - (I) is useful for immunizing a mammal to raise an immune response to an antigen by co-administering a nucleic acid encoding an antigen and a solid microsphere comprising an encapsulated cytokine (claimed). This immunization method is useful for modulating immune response against HIV-infection.

ADVANTAGE - Microsphere controlled-release formulation of cytokines maintains a high level of cytokines at the vaccination site for several days. The microspheres are stable in plasma and can be lyophilized without loss of bioactivity. Rate and duration of cytokine delivery can be varied by changing the properties of the microspheres.

Dwg.0/6

FS CPI

FA AB; DCN

MC CPI: B04-C02; B04-E02; B04-E03; **B04-G01**; B04-H02D; B04-H02N; B04-H04C; B04-H05C; B04-H08; **B04-H20**; B04-J01; B14-A02B1; B14-S11; B14-S11A; B14-S11C; D05-H07; D05-H11; D05-H12A; D05-H12B

TECH UPTX: 20000907
TECHNOLOGY FOCUS - ORGANIC CHEMISTRY - Preferred Composition: (I) comprises gelatin or chitosan. A cell targeting ligand is attached to the microsphere by glutaraldehyde cross-linking. (I) further comprises an encapsulated antigen.

TECHNOLOGY FOCUS - POLYMERS - Preferred Cation: The polymeric cation is preferably gelatin which is present at a concentration of 2-7 % in the step of coacervation.

TECHNOLOGY FOCUS - BIOTECHNOLOGY - Preferred Cytokine: The cytokine

encapsulated in (I) is preferably granulocyte macrophage-colony stimulating factor, tumor necrosis factor-alpha, interleukin (IL)-12, IL-4, gamma-interferon (gamma-INF) or their combinations. Preferred Method: (II) further comprises cross-linking a cell targeting ligand (preferably antibodies, hormones, **cell-adhesion molecules**, saccharides, drugs which bind to cellular receptors and neurotransmitters to the microsphere). Coacervation is performed in the presence of sodium sulfate (7-43 mM).

ABEX

ADMINISTRATION - Microspheres are administered by injection into the muscle, by subcutaneous injection or by bombardment with the microspheres from a high pressure gene gun (claimed). No specific dosage is given.

L83 ANSWER 13 OF 41 WPIX (C) 2002 THOMSON DERWENT
AN 2000-367636 [32] WPIX
DNC C2000-111138
TI Use of histamine-added immunoglobulin for inhibiting the expression of **cell adhesion molecules** for treating e.g. encephalitis, nephritis, myocarditis and vasculitis.
DC B03
IN NAIKI, M
PA (NIHZ) NIPPON ZOKI PHARM CO LTD
CYC 30
PI EP 1002545 A1 20000524 (200032)* EN 10p A61K039-395 <--
R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT RO SE SI
JP 2000143537 A 20000523 (200033) 5p A61K039-395 <--
AU 9958281 A 20000601 (200035) A61K039-395 <--
CA 2289329 A1 20000513 (200040) EN A61K039-395 <--
CN 1253833 A 20000524 (200043) A61K039-395 <--
KR 2000035446 A 20000626 (200111) A61K039-39 <--
ADT EP 1002545 A1 EP 1999-122027 19991112; JP 2000143537 A JP 1998-324013 19981113; AU 9958281 A AU 1999-58281 19991104; CA 2289329 A1 CA 1999-2289329 19991110; CN 1253833 A CN 1999-123486 19991112; KR 2000035446 A KR 1999-50174 19991112
PRAI JP 1998-324013 19981113
IC ICM **A61K039-39**; **A61K039-395**
ICS A61K031-415; **A61K047-48**; A61P037-02; A61P037-08; A61P043-00
ICI A61K031:415, **A61K039-395**
AB EP 1002545 A UPAB: 20000706
NOVELTY - Use of histamine-added immunoglobulin (I) to suppress the expression of **cell adhesion molecules**, is new.
ACTIVITY - Antiinflammatory.
USE - Histamine-added immunoglobulin is used to prevent or treat encephalitis, nephritis, myocarditis, vasculitis, enteritis, pneumonia or systemic inflammatory response syndrome (SIRS) (claimed).
Dwg.0/1
FS CPI
FA AB; DCN
MC CPI: **B04-G01**; B07-D09; B14-C03; B14-E10; B14-F01B; **B14-F02**; B14-J01; B14-J01B3; B14-K01; B14-N10
TECH UPTX: 20000706
TECHNOLOGY FOCUS - PHARMACEUTICALS - Preferred Materials: The ratio of components in (I) is 1-200 (preferably 5-50, more preferably 12) mg of immunoglobulin to 0.01-2 (preferably 0.05-0.5, more preferably 0.15) microg of histamine. The immunoglobulin component is human immunoglobulin and the histamine component is histamine dihydrochloride. (I) is formulated as an injectable composition.

ABEX

ADMINISTRATION - Dosage is 1-300 (preferably 5-150) mg once or several times a week by hypodermic injection.

L83 ANSWER 14 OF 41 WPIX (C) 2002 THOMSON DERWENT
AN 2000-339492 [29] WPIX
DNN N2000-254915 DNC C2000-102962
TI New artificial antigen presenting cells useful for isolating and expanding T cells, and modulating T cell responses for the treatment of e.g. autoimmune diseases, allergies.
DC B04 D16 S03
IN ALBANI, S
PA (ALBA-I) ALBANI S
CYC 90
PI WO 2000023053 A2 20000427 (200029)* EN 179p A61K009-127 <--
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW NL OA PT SD SE SL SZ TZ UG ZW
W: AE AL AM AT AU AZ BA BB BG BR BY CA CH CN CR CU CZ DE DK DM EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW
AU 2000011293 A 20000508 (200037) A61K009-127 <--
EP 1123086 A2 20010816 (200147) EN A61K009-127 <--
R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT RO SE SI
ADT WO 2000023053 A2 WO 1999-US24666 19991019; AU 2000011293 A AU 2000-11293 19991019; EP 1123086 A2 EP 1999-955116 19991019, WO 1999-US24666 19991019
FDT AU 2000011293 A Based on WO 200023053; EP 1123086 A2 Based on WO 200023053
PRAI US 1998-105018P 19981020
IC ICM **A61K009-127**
ICS **A61K047-48**; C07K014-705; G01N033-569
AB WO 200023053 A UPAB: 20000617
NOVELTY - Artificial antigen presenting cells (APC) comprising combinations of MHC:antigen complex with accessory molecules, co-stimulatory molecules, adhesion molecules, cell modulation molecule, irrelevant molecule, cholesterol, or solid support components, are new.

DETAILED DESCRIPTION - Artificial APCs comprising liposome, MHC, antigen, and accessory molecule components in combination with at least one of the following components: co-stimulatory molecule, cell modulation molecule, adhesion molecule, irrelevant molecule, cholesterol, or solid support components, the antigen component is in contact with at least the MHC component, the MHC and accessory components are in contact with at least one of the components, and the accessory molecule components provide for a stabilizing property to an interaction between a T cell receptor and MHC and antigen compounds.

INDEPENDENT CLAIMS are also included for the following:

(1) a method of making an artificial antigen presenting cell comprising:

(a) obtaining an MHC:antigen complex of interest;

(b) contacting the complex with a lipid and cholesterol, and forming a lipid membrane-associated the complex; and

(c) contacting the membrane-associated MHC:antigen complex with a molecule of interest selected from an accessory molecule, a co-stimulatory molecule, a cell modulation molecule, an adhesion molecule, an irrelevant molecule, cholesterol, GM-1 protein, cholera toxin beta subunit protein or a label;

(2) a method of identifying T cells specific for an antigen of interest comprising:

(a) obtaining a biological sample containing T cells specific for an antigen of interest;

(b) preparing an artificial APC, which contain the antigen;

(c) contacting the biological sample with the APC to form an artificial APC:T cell complex; where at least one element of the artificial antigen presenting cell is associated with a label, the element is selected from the antigen, an irrelevant molecule, a lipid layer, a lipid, an MHC molecule component, a co-stimulatory component, a cell modulation component, or an accessory molecule component; and

(d) detecting the label;

(3) a method of isolating T cells specific for an antigen of interest by employing the steps of (3a-c), removing the artificial APC:T cell complex from the biological sample; and separating T cells specific for the antigen from the artificial APC:T cell complex;

(4) a method of modulating T cell response by isolating T cells specific for an antigen of interest employing the method of (9); and contacting the isolated T cells with an artificial APC which has the antigen or its homologue, the artificial APC further having at least one molecule selected from an accessory molecule component, a co-stimulatory component, an adhesion component or a cell modulation component;

(5) methods of treating a condition in a subject which would be benefited by altering the functional pattern of cytokine production by certain antigen-specific T cells to increase or decrease Th-2 or Th-1 response comprising:

(a) isolating T cells specific for an antigen capable of triggering a Th-1 or Th-2 response upon recognition of the antigen by the subject's T cells; and

(b) combining the isolated T cells with an artificial APC having an MHC component capable of binding the antigen and a co-stimulatory molecule component comprising B7-2 or B7-1;

(6) a kit for isolation and/or modulation of T cells specific for an antigen of interest comprising artificial APCs, solid supports, reagents or an immunomodulatory column device;

(7) an immunomodulatory column comprising a multiple compartments having a channel interconnecting adjacent compartments, positioned in relation to one another in series, the channels having a means to isolate these compartments from one another, where the compartments further have at least one entrance and exit port for receiving or expelling, respectively, a flowable medium, the ports have a means to close to impede the flowable medium, and the compartments is optionally comprised of the components solid supports or artificial APCs.

ACTIVITY - Cytostatic; anti-sclerotic; anti-allergic; antiarthritic; antiviral; immunosuppressive.

MECHANISM OF ACTION - T cell response modulator.

USE - Artificial APCs may be used for isolating T cells specific for an antigen of interest, as well as for modulating and modifying T cell responses. These may also be used for the treatment of a condition in an individual who would be benefited by modulating the functional pattern of active factors expressed by a T cell. Conditions which may be improved by altering the functional pattern of response toward a Th2 response include e.g. type 1 diabetes mellitus, multiple sclerosis rheumatoid arthritis, juvenile rheumatoid arthritis dermatomyositis, and uveitis, cancer, viral or bacterial infection, an autoimmune disease or an allergy (to dust, animal skin bypass products, vegetables, fruits, pollen or chemicals). The APCs are useful for manipulating the T cell responses by which treatment can be provided for numerous disease states.

ADVANTAGE - The present invention is more versatile compared with prior arts. It is not concerned with detecting natural APCs, instead directed to the isolation and manipulation of antigen-specific T cells. The use of co-stimulatory, adhesion and other accessory molecules in a free floating format helps to both anchor and direct the interaction between MHC:antigen:accessory molecule and T cell receptors by providing a means by which T cells in the sample will be represented with a structure more similar with that found in the natural state. The free floating MHC component is able to participate in the migration or concentration of complexes in capping which is important to improved binding and activation of bound t cells. Moreover, no cell proliferation is necessary to identify and isolate antigen-specific T cells. Addition of accessory molecules allows for substantially improved binding associated and manipulation of T cells important in the identification and stimulation of antigen-specific T cells.

Dwg.0/24

FS CPI EPI
FA AB; DCN
MC CPI: B01-D02; **B04-B04C**; B04-B04D4; B04-B04D5; B04-E05; B04-F01; B11-C07A3; B11-C07A5; B11-C08D; B11-C08E3; B11-C08E5; B12-K04; B14-A01; B14-A02; B14-C09B; B14-G02; B14-G02A; B14-G02D; **B14-H01**; B14-S01; B14-S04; D05-H07; D05-H09; D05-H10; D05-H11; D05-H12D1; D05-H14; D05-H18B
EPI: S03-E04D; S03-E09C; S03-E14H4; S03-E14H5
TECH UPTX: 20000617
TECHNOLOGY FOCUS - BIOTECHNOLOGY - Preferred Cell Components: The liposome components of the APC comprise a lipid selected from a phospholipid, a neutral phospholipid, or a phosphotidylcholine. The surfactant component is cholesterol, which is in contact with at least the liposome components. The label, which may consist of biotin, vancomycin, a fluorochrome, FITC, or a radiolabel, is associated with at least the lipid bilayer of the liposome components, a lipid of the liposome components, an antigen component, an MHC component, or an accessory component. The antigen presented by an MHC component for contact with and recognition by a T cell receptor may consists of a peptide, a peptide derived from the recipient for graft versus host disease, a cancer cell-derived peptide, a peptide derived from an allergen, a donor-derived peptide, a pathogen-derived molecule, a peptide derived by epitope mapping, a self-derived molecule, or a self-derived molecule that has sequence identity with the pathogen-derived antigen. The sequence identity may have a range of 5-100 (especially 50-100) %. The accessory molecule component is an LFA-1, CD11a/18, CD54(**ICAM-1**), CD106(**VCAM**), CD49d/29(VLA-4), or antibodies to the ligands of these molecules. The solid support is may be a glass bead 25-300 mum in diameter, or a magnetic bead 25-300 mum in diameter. Preferably, the lipid-coated solid support further comprises capture molecules capable of binding to the irrelevant molecule, and is non-covalently associated with the lipid.
ABEX
EXAMPLE - Complexes of affinity-purified MHC molecules I-As and I-Ad (each expressed in a B cell lymphoma and purified via immunoaffinity column) were inserted into liposomes by a 72 hour 4 degreesC dialysis against 3 changes of PBS at a 1:10 molar ratio of MHC to liposomes, and the control peptide (b-peptides) were incubated with the liposome:MHC complexes for 18 hours at room temperature to form liposome:MHC:b-peptide complexes. The OVA323-326 peptide and the control peptide, Hi15, were biotinylated, and the biotinylated peptides (b-peptides) were incubated with the liposome:MHC complexes to form liposome:MHC:b-peptide complexes. Viable cells were incubated with antibodies anti-CD3e, anti-CDCD4, anti-CD8, anti-HAS, and anti-CD69. Liposome:MHC:b-peptide complexes were preincubated in fluorescent streptavidin molecule. Bulk-sorted cells used for reanalysis were incubated to remove liposome:MHC:b-peptide complexes, prior to restaining with liposome:MHC and a different b-peptide. Single sorts were dispersed in 96-well culture plates containing fresh irradiated antigen-presenting cells obtained from syngeneic BALB/c mouse spleen. 8-12 wells showed proliferation over 6 weeks. Specific recognition of MHC/peptide complexes by T-T hybridomas AG111.207 (I-As/OVA323-326 specific) and 8D051.15 (Iad/OVA323-326 specific) were observed.

L83 ANSWER 15 OF 41 WPIX (C) 2002 THOMSON DERWENT
AN 2000-273125 [24] WPIX
DNC C2000-083484
TI Stabilized protein compositions comprise protein and stabilizing buffer, used to treat or prevent mastitis, metritis or bovine respiratory disease in cattle and to maintain therapeutic levels of protein.
DC B04 C03
IN CANNING, P C; KAMICKER, B J; KASRAIAN, K
PA (PFIZ) PFIZER PROD INC
CYC 33
PI EP 988861 A1 20000329 (200024)* EN 46p A61K038-18

R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT RO SE SI

AU 9944501	A	20000309 (200024)			A61K038-18	
JP 2000063264	A	20000229 (200024)		30p	A61K009-08	<--
CA 2280449	A1	20000217 (200031)	EN		A61K038-27	
CN 1250668	A	20000419 (200036)			A61K038-18	
BR 9904150	A	20001226 (200103)			A61K038-27	
NZ 337258	A	20010427 (200128)			A61K047-20	<--
ZA 9905201	A	20010425 (200128)		59p	C07K000-00	
MX 9907663	A1	20000901 (200139)			A61K047-42	<--

ADT EP 988861 A1 EP 1999-306262 19990806; AU 9944501 A AU 1999-44501 19990816; JP 2000063264 A JP 1999-230853 19990817; CA 2280449 A1 CA 1999-2280449 19990813; CN 1250668 A CN 1999-122020 19990817; BR 9904150 A BR 1999-4150 19990817; NZ 337258 A NZ 1999-337258 19990816; ZA 9905201 A ZA 1999-5201 19990816; MX 9907663 A1 MX 1999-7663 19990817

FDT NZ 337258 A Div in NZ 510140

PRAI US 1998-96876P 19980817

IC ICM **A61K009-08**; A61K038-18; A61K038-27; **A61K047-20**; **A61K047-42**; C07K000-00

ICS **A61K009-10**; A61K038-00; A61K038-19; A61K038-20; **A61K039-00**; **A61K039-385**; **A61K039-395**; **A61K047-16**; **A61K047-18**; **A61K047-22**; A61P015-14; A61P031-00

AB EP 988861 A UPAB: 20000522

NOVELTY - Stabilized protein compositions (I) comprise a protein and a stabilizing buffer. The compositions are capable of maintaining therapeutic levels of the protein for a sustained period of time.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following:

(1) a dosage form of (I) for parenteral administration, where the protein is present in an amount sufficient to provide therapeutic benefit to a mammal for a predetermined period of time;

(2) a stabilized protein composition (II) comprising bovine G-CSF and HEPES buffer and which is capable of providing an extended shelf life of from 3 weeks to 18 months;

(3) a kit for administering (I) to mammals comprising a first container containing the protein and a second container containing the buffer, where when the protein is combined with the buffer, the composition is capable of maintaining therapeutic levels of the protein in the mammal for a sustained period of at least 3 days.

ACTIVITY - Antibacterial; antiinflammatory.

MECHANISM OF ACTION - Granulocyte colony-stimulating.

The in vivo activity of bovine G-CSF formulated in 1M HEPES was compared with control formulation containing 5% mannitol, 10 mM acetate buffer and Tween 80 (RTM: Polysorbate 80) at pH 4.0. For the control formulation, the white blood count (WBC) stayed above threshold value of 200% of baseline level (level associated with protection against infection) for only about 24-30 hours. When bovine G-CSF was formulated in 1M N-(2-hydroxyethyl)piperazine-N'-(2-ethanesulfonic acid) (HEPES), the polymorphonuclear numbers remained above threshold for a minimum of 3 days or 72 hours.

USE - The compositions are used for sustained administration of proteins such as colony-stimulating factors (G-CSF), somatotropins, cytokines, antibodies and antigens as well as activins, adhesion molecules (L-**selectin**, CD-18, **intercellular adhesion molecule-1**), chemokines, chemotactic factors, erythropoeitin, growth factor, inhibins, insulin, interferons (alpha , beta , gamma), interleukins (1-18), leptin, macrophage inflammatory proteins, macrophage migration inhibitor factor, macrophage stimulating protein, neurotrophins, neutrophils inhibitor factor, oncostatins, somatostatins, stem cell factors, tumor necrosis factors, thrombopoetins and their cell-associated and soluble receptors. They are used for the treatment or prevention of mastitis, metritis or bovine respiratory

disease in cattle (claimed) such as mastitis associated with Staphylococcus aureus, Escherichia coli, Streptococcus uberis, Strep. dysgalactiae, Strep. agalactiae, Klebsiella spp., Corynebacterium spp., bovine respiratory disease associated with infectious bovine rhinotracheitis virus, parainfluenza virus (P13), bovine viral diarrhea virus, Pasteurella haemolytica, **P.** multocida and Haemophilus somnus, reproductive disorders such as metritis, and bovine diarrhea associated with **E.** coli and Eimeria spp. as well as infectious diseases of dogs such as pyoderma and respiratory disease in dogs such as kennel cough. They may also be used in cats and dogs to ameliorate chemotherapy-induced myelosuppression and to allow for more aggressive cancer treatment protocols. They are used to treat humans, cattle, swine, horses, goats, sheep, cats and dogs.

ADVANTAGE - The compositions are capable of maintaining therapeutic levels of the protein for a sustained period of time such as at least 3 days in vivo and in vitro. The compositions have extended shelf-lives of 3 weeks-18 months. The compositions are sterile, well tolerated by mammals without induction of appreciable swelling, pain or necrosis at the injection site.

Solutions containing bovine G-CSF (0.1 mg/ml) were prepared in the buffers TES, HEPES and TRICINE at concentrations of 0.1M, 1M and 2M. Each formulation (1 ml) was placed in a 1-ml vial and placed in an oven at 40 deg. C for 9 days. Samples were removed from each vial every 3 days and analyzed by size exclusion high-performance liquid chromatography (SEC-HPLC). The percentage recovery (remaining) of 0.1 mg/ml bovine G-CSF solutions was determined. The percentage recovery at 0, 3, 6 and 9 days, respectively, were as follows (%): HEPES: 0.1M = 100, 15, 9, 5; 1M = 100, 95, 96, 95; 2M = 100, 78, 82, 83; TES: 0.1M = 100, 16, 11, 9; 1M = 100, 85, 97, 93; 2M = 100, 100, 98, 98; and TRICINE: 0.1M = 100, 17, 10, 5; 1M = 100, 85, 79, 70; 2M = 100, 94, 88, 86. The results showed that the presence of buffers significantly maintained the activity of bovine G-CSF for sustained periods from 3-9 days.

DESCRIPTION OF DRAWING(S) - Plot of white-blood cells versus time past injection (hours) for bovine G-CSF formulated in 1M HEPES versus a control formulation.

Dwg.1/29

FS CPI

FA AB; GI; DCN

MC CPI: **B04-B04C**; **B04-G01**; B04-H04A; B04-H04B; B04-H07; B04-H08; B04-J03A; B04-J05J; B04-N02; B07-D11; B10-A09B; B10-B01B; B12-M10A; B14-A01; B14-A02; B14-C03; B14-E02; B14-K01; B14-K01B; B14-N14; **C04-B04C**; **C04-G01**; C04-H04A; C04-H04B; C04-H07; C04-H08; C04-J03A; C04-J05J; C04-N02; C07-D11; C10-A09B; C10-B01B; C12-M10A; C14-A01; C14-A02; C14-C03; C14-E02; C14-K01; C14-K01B; C14-N14

TECH UPTX: 20000522

TECHNOLOGY FOCUS - PHARMACEUTICALS - Preferred Compositions: In (I), the proteins are colony-stimulating factors (preferred), somatotropins, cytokines, antibodies and antigens, preferably human granulocyte colony-stimulating factor (G-CSF), bovine G-CSF (preferred) or canine G-CSF. The compositions are at physiological pH, preferably 4.0-7.5. The compositions are at physiological temperature. The stabilizing buffer is N-(2-hydroxyethyl)piperazine-N'-(2-ethanesulfonic acid) (HEPES), N-tris-(hydroxymethyl)aminomethane(hydroxymethyl)-methyl-2-aminoethanesulfonic acid (TES) or N-tris-(hydroxymethyl)aminomethane(hydroxymethyl)methylglycine (TRICINE). The sustained period is at least 3 days, preferably in vivo. The G-CSF is present at a concentration of 0.01-6 mg/ml. The stabilizing buffer is present at a concentration of 0.05-2M. The stabilizing buffer is preferably HEPES at a concentration of 1M. In (II), the HEPES buffer is at 0.05-2M, the pH of the composition is 7.5 and the temperature is less than 40 (preferably less than 4) degreesC. Preferred Dosage Form: The protein is bovine G-CSF present at 0.01-5 mg/ml; the stabilizing buffer is HEPES, TES or TRICINE and is especially

HEPES at 0.05-2M; the mammal is a cow; the predetermined period of time is at least 3 days and the composition is at a pH of 7.5. The dosage form further comprises surfactant and viscosity modifiers.

ABEX

ADMINISTRATION - Administration is parenteral, oral, nasal, by inhalation, intraocular, intradermal or by infusion. In the parenteral dosage form in (1), the bovine G-CSF is administered at 0.1-50 microg/kg (claimed). Dosage forms contain 0.1-50 (preferably 1-25 (especially 3-25, particularly 24) microg/kg of bovine G-CSF. The dose is effective for at least 3 days.

L83 ANSWER 16 OF 41 WPIX (C) 2002 THOMSON DERWENT
AN 2000-182177 [16] WPIX
DNC C2000-056890
TI Binding ligand for aminophospholipid used in the treatment of vascularized tumors, comprises targeting component and therapeutic agent.
DC B04 D16 K08
IN RAN, S; THORPE, P E
PA (TEXA) UNIV TEXAS SYSTEM
CYC 87
PI WO 2000002587 A1 20000120 (200016)* EN 265p A61K047-48 <--
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW NL OA PT SD SE SL SZ UG ZW
W: AE AL AM AT AU AZ BA BB BG BR BY CA CH CN CU CZ DE DK EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT UA UG UZ VN YU ZA ZW
AU 9950958 A 20000201 (200028) A61K047-48 <--
BR 9912053 A 20010403 (200128) A61K047-48 <--
EP 1098665 A1 20010516 (200128) EN A61K047-48 <--
R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT RO SE SI
US 6312694 B1 20011106 (200174) A61K039-395 <--
MX 2001000455 A1 20010501 (200227) A61K047-48 <--
ADT WO 2000002587 A1 WO 1999-US15668 19990712; AU 9950958 A AU 1999-50958 19990712; BR 9912053 A BR 1999-12053 19990712, WO 1999-US15668 19990712; EP 1098665 A1 EP 1999-935491 19990712, WO 1999-US15668 19990712; US 6312694 B1 Provisional US 1998-92589P 19980713, Provisional US 1998-110600P 19981202, US 1999-351457 19990712; MX 2001000455 A1 MX 2001-455 20010112
FDT AU 9950958 A Based on WO 200002587; BR 9912053 A Based on WO 200002587; EP 1098665 A1 Based on WO 200002587
PRAI US 1998-110600P 19981202; US 1998-92589P 19980713; US 1999-351457 19990712
IC ICM **A61K039-395; A61K047-48**
ICS A61K049-00; A61K049-04; A61K051-10; C07K016-00; C12P021-08
AB WO 200002587 A UPAB: 20000330
NOVELTY - Binding ligand (I) comprising a targeting agent (II) that binds to an aminophospholipid (APL) linked to a therapeutic agent (III), is new.
DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following;
(a) pharmaceutical composition containing (I);
(b) kits comprising (I), or the composition of (a), plus a construct containing a detectable agent linked to a second (II) that binds to APL;
(c) treatment of vascularized tumors by administering (I) in which (II) binds to an APL on the luminal surface of blood vessels in a tumor, optionally after imaging with the construct of (b) and/or in combination with a second anticancer agent (III);
(d) imaging of vascularized tumors by administering at least one (I) containing a detectable agent linked to (II) that binds to APL on the luminal surface of blood vessels in the tumor.
ACTIVITY - Anticancer.
MECHANISM OF ACTION - (I) induce coagulation (thrombosis) in tumor

vasculature or cause tumor necrosis (possibly by cell- or complement-mediated cytotoxicity and/or apoptosis). The method is based on the observation that phosphatidylethanolamine (PE) and phosphatidylserine (PS) are stable and specific markers of tumor blood vessels that are transported to the cell surface independently of apoptosis or other cell-death mechanisms.

USE - (I) are used to treat vascularized tumors, malignant or benign, in animals, most especially large tumors. A conjugate (10 micro g) of annexin (specific for phosphatidylserine) and truncated tissue factor was administered intravenously to nu/nu mice carrying human HT29 colorectal carcinomas of about 1.2 cubic cm. After 24 hr, the animals were killed and analyzed. The conjugate had induced significant blood vessel coagulation in the tumors, with about 55% of such vessels having undergone thrombosis.

ADVANTAGE - Ab provide a highly specific method of destroying tumor vasculature. Endothelial cells in normal blood vessels are not affected. Ab induce tumor regression, rather than just stasis, as is the case with anti-angiogenic agents that inhibit proliferation of tumor-associated blood vessels.

Dwg.0/4

FS CPI

FA AB; DCN

MC CPI: B04-A07A; B04-E02A; B04-E08; B04-F02; B04-F04; B04-F05; **B04-G01**; B04-H19; **B04-H20**; B04-M01; B11-C07A3; B11-C07A6; B11-C08A; B12-K04C2; B12-K07; B12-M05; B14-C03; B14-C09; B14-F01E; **B14-H01B**; **B14-N03**; B14-N14; **B14-S03**; B14-S04; D05-H11; K09-B

TECH UPTX: 20000330

TECHNOLOGY FOCUS - PHARMACEUTICALS - Preferred Targeting Agent: Comprises;
(i) an anti-APL antibody (Ab) or its fragments;
(ii) a phosphatidylserine (PS)-binding protein or its fragment, particularly an annexin;
(iii) a phosphoethanolamine (PE)-binding protein or its fragment, particularly a kininogen.
(II) has 2,3 or more binding sites for APL, may be recombinant and particularly binds PS or PE.
Preferred Materials: (III) are;
(i) an anticellular or cytotoxic agent, **e**.g. a steroid, cytokine, antimetabolite, Vinca alkaloid, alkylating agent, DNA synthesis inhibitor etc.;
(ii) a toxin of plant, fungal or bacterial origin, particularly (deglycosyalated) ricin A chain;
(iii) a coagulant, **e**.g. factors II or X (optionally activated), Russell's viper venom, thromboxan A2 etc.; or
(iv) a tissue factor (or its multimers, mutants or derivatives).
Optionally more than one (III) is attached, either directly (via a covalent bond, chemical crosslinking or as a recombinant fusion protein) or indirectly through an antibody or its fragment. Particularly in the last case, (I) is a bispecific antibody comprising a targeting component linked to a second antibody that binds (III). The label present in imaging agents is;
(i) detectable by X-rays, **e**.g. bismuth or gold;
(ii) radioactive, **e**.g. copper 67, indium 111, iodine 125, technetium 99m etc.; or
(iii) detectable by nuclear magnetic spin resonance, **e**.g. cobalt (II), gadolinium (III), terbium (III) etc.
Suitable (III) are chemotherapeutic, radiotherapeutic, anti-angiogenic or apoptosis-inducing agents, and may comprise an antibody-therapeutic agent construct consisting of a targeting antibody (tAb) that binds a surface-expressed, -accessible or - localized component of tumor cells, stroma or vasculature. Particularly tAB is directed to a cell-surface tumor antigen, stroma component or surface cytokine- or coagulation-induced component of blood vessels, **e**.g. (I), transforming growth factorbeta receptor, **selectin**, adhesion

molecule etc. Alternatively (IV) is a naked antibody, or fragment, that binds APL.
Preferred Compositions: These may contain two (I) that bind to different APL and are formulated for intravenous administration. They may also include a (IV).

TECHNOLOGY FOCUS - BIOLOGY - Preparation: Ab-producing cells are;
(i) cells from a human patient having a disease associated with production of Ab;
(ii) produced by in vitro stimulation of a mixed population of human peripheral blood lymphocytes with (I); or
(iii) are produced by immunizing a non-human animal (particularly a transgenic mouse carrying a human antibody library) with (I).
The Ab-producing cells are then fused conventionally to generate Ab-expressing hybridomas.

TECHNOLOGY FOCUS - BIOTECHNOLOGY - Preparation: Ab may also be prepared by;
(i) recombinant expression of Ab-encoding nucleic acid, isolated from Ab-expressing cells isolated as above; or
(ii) immunizing an animal with (I), preparing a combinatorial Ig phagemid library expressing RNA isolated from the animal's spleen, selecting a clone that expresses Ab, and expressing Ab-encoding DNA from this clone.

ABEX

WIDER DISCLOSURE - (I) may also be used to treat other diseases where prothrombotic blood vessels are a contributory factor, e.g. diabetic retinopathy, restenosis, arthritis, inflammatory diseases, endometriosis etc.

SPECIFIC COMPOUNDS - (I) comprises an anti-phosphatdylserine antibody (or its fragment) attached (in)directly to truncated tissue factor.

ADMINISTRATION - (I) are particularly given by intravenous injection, but also contemplated are other routes of injection, transdermal delivery, implantation of antibody-expressing cells or expression from gene therapy vectors. Generally doses are 1-500 mg, typically 10-100 mg 3 times within 7 days, optionally in combination with other anticancer treatments. Doses of imaging agent are 0.1-10 mg.

L83 ANSWER 17 OF 41 WPIX (C) 2002 THOMSON DERWENT
AN 2000-182175 [16] WPIX
DNN N2000-134466 DNC C2000-056888
TI New composition for killing tumor vascular endothelial cells for treating solid tumors, comprises unconjugated anti-aminophospholipid antibody.
DC B04 D16 K08 P14
IN RAN, S; THORPE, P E
PA (TEXA) UNIV TEXAS SYSTEM
CYC 87
PI WO 2000002584 A2 20000120 (200016)* EN 225p A61K039-395 <--
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW NL OA PT SD SE SL SZ UG ZW
W: AE AL AM AT AU AZ BA BB BG BR BY CA CH CN CU CZ DE DK EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT UA UG UZ VN YU ZA ZW
AU 9954585 A 20000201 (200028) A61K039-395 <--
EP 1096955 A2 20010509 (200128) EN A61K039-395 <--
R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT RO SE SI
MX 2001000457 A1 20010501 (200227) A01K067-027
US 6406693 B1 20020618 (200244) A61K039-395 <--
ADT WO 2000002584 A2 WO 1999-US15600 19990712; AU 9954585 A AU 1999-54585 19990712; EP 1096955 A2 EP 1999-940802 19990712, WO 1999-US15600 19990712;

MX 2001000457 A1 MX 2001-457 20010112; US 6406693 B1 Provisional US 1998-92672P 19980713, Provisional US 1998-110608P 19981202, US 1999-351543 19990712

FDT AU 9954585 A Based on WO 200002584; EP 1096955 A2 Based on WO 200002584

PRAI US 1998-110608P 19981202; US 1998-92672P 19980713; US 1999-351543 19990712

IC ICM **A61K039-395**
ICS **A61K047-48**; A61K051-10; C07K016-30; C12Q001-68

ICA A01K067-027; C07K016-00; C07K016-28

ICI A01K067-027, C07K016:00, C07K016:28

AB WO 200002584 A UPAB: 20000330
NOVELTY - A composition (I) comprising an anti-aminophospholipid antibody (II), or its antigen-binding region, for killing tumor vasculature endothelial cells, is new.

DETAILED DESCRIPTION - An INDEPENDENT CLAIM is also included for kits comprising (II) plus a detectably labeled antibody, or its fragment, that binds to an aminophospholipid and/or a second anticancer agent (III).

ACTIVITY - Anticancer.

MECHANISM OF ACTION - (II) induce coagulation (thrombosis) in tumor vasculature or cause tumor necrosis (possibly by cell or complement-mediated cytotoxicity and/or apoptosis). The method is based on the observation that phosphatidylethanoloamine (PE) and phosphatidylserine (PS) are stable and specific markers of tumor blood vessels that are transported to the cell surface independently of apoptosis or other cell-death mechanisms.

USE - (I) are used to treat malignant or benign vascularized tumors in animals (claimed), especially large tumors.

ADVANTAGE - (I) provides a safe and effective method of destroying tumor vasculature, and since unconjugated antibodies are used, the method is simple without the need to prepare conjugates. Endothelial cells in normal blood vessels are not affected. (II) induce tumor regression, rather than just stasis, as is the case with anti-angiogenic agents that inhibit proliferation of tumor-associated blood vessels.

Dwg.0/4

FS CPI GMPI

FA AB; DCN

MC CPI: B04-F01; **B04-G01**; B11-C07A; B12-K04A; B14-C03; B14-C09; B14-F01; **B14-H01B**; **B14-N03**; B14-N14; B14-S04; D05-H09; D05-H11A1; D05-H11A2; D05-H17B1; D05-H17C1; K08-A; K09-B

TECH UPTX: 20000330
TECHNOLOGY FOCUS - PHARMACEUTICALS - Preferred Antibody: (II) is an immunoglobulin (Ig) G or M antibody, and suitable fragments are (single-chain) Fv, Fab', Fab or F(ab')2. It is preferably monoclonal and may be human, humanized or part-human chimeras, optionally in dimeric, trimeric or multimeric forms. (II) especially bind to phosphatidylethanolamine (PE) or phosphatidylserine (PS) on the luminal surface of blood vessels in the tumor.
Preferred Kit: Kits contain at least two (II), specific for different (I). Kits may contain (II) and (III) in separate formulations or as a single product.
Preferred Materials: The labels in the labeled antibody are detectable by X-rays, such as bismuth or gold, radioactive, **e**.g. copper67, indium111, iodine 125 or technetium99m, or are detectable by nuclear magnetic spin resonance, **e**.g. cobalt(II), gadolinium(III), terbium(III). Suitable (III) are chemotherapeutic, radiotherapeutic, anti-angiogenic or apoptosis-inducing agents, and may comprise an antibody-therapeutic agent construct consisting of a targeting antibody (tAb) that binds a surface-expressed, accessible or localized component of tumor cells, stroma or vasculature. Particularly tAB is directed to a cell-surface tumor antigen, stroma component or surface cytokine or coagulation-induced component of blood vessels, such as transforming growth factorbeta receptor, **selectin** or adhesion molecules. The agent linked to tAb is a cytotoxin, derived from plants, fungi or

bacteria, particularly deglycosylated ricin A chain. Alternatively the agent is a coagulation factor such as (truncated) tissue factor or its derivatives, or an antibody that binds a coagulation factor.

TECHNOLOGY FOCUS - BIOLOGY - Preparation: Antibody (II)-producing cells are cells from a human patient having a disease associated with production of (II), are produced by in vitro stimulation of a mixed population of human peripheral blood lymphocytes with (I) or are produced by immunizing a non-human animal (particularly a transgenic mouse carrying a human antibody library) with (I). The (II)-producing cells are then fused conventionally to generate (II)-expressing hybridomas.

TECHNOLOGY FOCUS - BIOTECHNOLOGY - Preparation: (II) may also be prepared by recombinant expression of a nucleic acid encoding (II), isolated from cells expressing (II) isolated as above or by immunizing an animal with (I), preparing a combinatorial Ig phagemid library expressing RNA isolated from the animal's spleen, selecting a clone that expresses (II), and expressing (II)-encoding DNA from this clone.

ABEX

WIDER DISCLOSURE - (I) may also be used to treat other diseases where prothrombotic blood vessels are a contributory factor, such as diabetic retinopathy, restenosis, arthritis, inflammatory diseases and endometriosis.

ADMINISTRATION - (I) are preferably administered by intravenous injection, but injection, transdermal delivery, implantation of cells expressing (II), or expression from gene therapy vectors is also possible. Dosage is 1 - 500 mg, preferably 10 - 100 mg 3 times within 7 days, optionally in combination with other anticancer treatments. Doses of the labeled antibody are preferably 0.1 - 10 mg.

EXAMPLE - Balb/c mice were injected subcutaneously with 107 Colo26 (syngeneic murine colorectal carcinoma) cells, and when the tumors were 0.6 - 0.9 cubic cm, they were injected intraperitoneally with 20 mug of an anti-phosphatidylserine antibody (IgM). Three doses were given over 48 hours and tumor growth was monitored. This treatment inhibited tumor growth by up to 60%, although tumor regrowth started 7 - 8 days after treatment. Analysis of the tumors showed vascular injury, thrombosis and necrosis, with evident clots and disintegration of tumor mass surrounding the blocked blood vessels.

L83 ANSWER 18 OF 41 WPIX (C) 2002 THOMSON DERWENT
AN 2000-105663 [09] WPIX
DNC C2000-031695
TI Use of compositions containing a receptor ligand and a receptor ligand binding molecule for treating e.g. infections, inflammatory or immune disease or disorder or cancers.
DC B04
IN BURNS, J M; DEVICO, A L; GALLO, R; LEWIS, G K
PA (UYMA-N) UNIV MARYLAND BIOTECHNOLOGY INST
CYC 87
PI WO 9962535 A2 19991209 (200009)* EN 70p A61K038-00
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW NL OA PT SD SE SL SZ UG ZW
W: AE AL AM AT AU AZ BA BB BG BR BY CA CH CN CU CZ DE DK EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT UA UG UZ VN YU ZA ZW
AU 9943254 A 19991220 (200021) A61K038-00
EP 1100527 A2 20010523 (200130) EN A61K038-19
R: AT BE CH CY DE DK ES FI FR GB GR IE IT LI LU MC NL PT SE
US 6399078 B1 20020604 (200242) A61K047-00 <--
ADT WO 9962535 A2 WO 1999-US12137 19990601; AU 9943254 A AU 1999-43254

19990601; EP 1100527 A2 EP 1999-955219 19990601, WO 1999-US12137 19990601; US 6399078 B1 Provisional US 1998-87436P 19980601, US 1999-323719 19990601

FDT AU 9943254 A Based on WO 9962535; EP 1100527 A2 Based on WO 9962535

PRAI US 1998-87436P 19980601; US 1999-323719 19990601

IC ICM A61K038-00; A61K038-19; **A61K047-00**

ICS A61K031-727; A61K038-17; **A61K039-00**; A61K045-00

AB WO 9962535 A UPAB: 20000218

NOVELTY - The use of compositions containing a receptor ligand (RL) and a receptor ligand binding molecule (RLBM) for treating diseases or conditions related to ligand/receptor signaling is new.

DETAILED DESCRIPTION - Method (I) of treating a disease or condition which is caused by or contributed to by the function of a ligand/receptor-mediated signaling pathway or which is dependent upon the extracellular recognition of a receptor by an infectious agent, comprises administering to a patient a composition which includes a RL, and a RLBM, where the composition is capable of antagonizing the function of the receptor or altering the extracellular recognition of the receptor by the infectious agent, to treat the disease or condition.

INDEPENDENT CLAIMS are also included for the following:

(1) a method (II) of inhibiting a chemokine receptor-mediated infection comprising contacting a cell with a formulation which includes a chemokine which binds to the chemokine receptor, and a chemokine binding molecule (CBM) which binds to the chemokine where the formulation is capable of inhibiting the chemokine receptor-mediated infection and suppressing signal transduction from the chemokine receptor; and

(2) a method (III) of treating or preventing infection of a subject by HIV comprising administering to the subject a composition which includes a chemokine and a CBM, where the composition resulting from the combination of the chemokine and the CBM confers a longer soluble plasma half-life upon the chemokine than the soluble plasma half-life of the chemokine when administered without the CBM and where the composition is further capable of suppressing signal transduction from a receptor to which the chemokine ordinarily binds;

ACTIVITY - Anti-microbial, immunomodulatory, neurotropic, catabolic, etc.

MECHANISM OF ACTION - Chemokine receptor antagonist by competitive inhibition thereby altering the extracellular recognition of the receptor by the infectious agent.

USE - The methods can be used for treating an infectious disease caused by a virus e.g. HIV, Epstein-Barr virus, rhinovirus, poliovirus, rabies virus, reovirus, influenza virus, herpes simplex virus, hepatitis virus, togavirus, varicella-zoster virus, paramyxovirus, cytomegalovirus, subacute sclerosing panencephalitis virus, adenovirus, poxvirus, reovirus, papovavirus, papillmavirus, polyomavirus, slow virus, or bacteria, e.g. Helicobacter pylori, Borelia burgdoferi, Legionella pneumophilia, Mycobacterium tuberculosis, M. avium M. intracellulare, M. kansaii, M. gordonae, M. leprae, Staphylococcus aureus, Neisseria gonorrhoeae, N. meningitidis, Listeria monocytogenes, S. pyogenes, S. agalactiae, S. faecalis, S. bovis, S. anginosus, S. pneumoniae, pathogenic Campylobacter species, pathogenic Enterococc us species, Harmophilus influenzae, Bacillus antracis, Corynebacterium diphtheriae, Enterobacter aerogenes, Klebsiella pneumoniae, pasturella multocide, pathogenic Bacteroides fragilis group species, Fusobacterium nucleatum, Streptobacillus moniliformis, treponema pallidium, Treponema pertenue, Leptospira, and Actimomyces isrealli, fungi, e.g. Cryptocossuc neoformans, Histoplasma capsulatum, Coccidioides immitis, Blastomyces dermatidis, Chlamydia trachomatis, and Candida albicans, or a microbe, e.g. Bacillus anthracis, a pathogenic Bordetella species, Bordetella pertussis, Clostridium botulinum, C. tetani, Vibrio cholerae, Corynebactreium diphtheriae, E. coli, Pseudomonase aeruginosa, and Shigella dysenteriae (claimed). They can also be used for treating an inflammatory or an immune disease or disorder (e.g. AIDS) or cancer (claimed). In particular, they can be used for treating e.g. systemic lupus erythematosus, glomerulonephritis,

vasculitis, pyogenic infections, immune complex disease, adult respiratory distress syndrome, septic shock or multiple organ failure, vascular diseases or disorders, cardiac disorders, cardiovascular system diseases and disorders, wound healing, limb regeneration, periodontal regeneration, neurological damage or diseases, e.g., Alzheimer's disease, Parkinson's disease, AIDS-related complex, cerebral palsy, depression or neuroendocrine disorders such as hyperthyroidism or hypertension, other diseases, conditions or disorders which result from aberrations or alterations of cell receptor-dependent processes including collateral growth and remodeling of cardiac blood vessels, angiogenesis, cellular transformation through autocrine or paracrine mechanisms, chemotactic stimulation of cells (e.g. endothelial), neurite outgrowth of neuronal precursor cell types (e.g. PC12 phaeochromoctoma). They can also be used for treating e.g. insulin-dependent hypoglycemic condition or amyloid diseases ad to promote skeletal muscle development thereby increasing muscle mass in livestock and obviating the need for excessive use of antibiotics and hormones to improve feed conversion and weight gain in animals. The methods can also be used in drug screening.

ADVANTAGE - The combination of the RL and the RLBM has a longer plasma half-life than the RL alone and provides more effective therapy. Since the complexes are unable to trigger receptors, they should prove to be free from undesirable side effects resulting from the continued activation of their target receptor as has been observed in the use of chemokines to block HIV infection.

Dwg.0/7

FS CPI

FA AB; DCN

MC CPI: B04-C02E; B04-C02F; B04-H02; B04-H08; B04-H13; **B04-H20**; B14-A01; B14-A02; B14-A04; B14-C03; B14-G01

TECH UPTX: 20000218

TECHNOLOGY FOCUS - BIOTECHNOLOGY - Preferred Method: The method (I) where the composition has a longer serum half-life than the receptor ligand alone.The RL may be a chemokine, especialy a human chemokine, e.g. an interleukin, a tumor necrosis factor, a lymphokine, an interferon, a lymphotoxin, MIP-1alpha, MIP1beta, RANTES, MDC, I-309, eptaxon, MCP-3, and SDF-1. The RLBM is a polyanionic molecule, preferably a glycosaminoglycan (natural or synthetic), e.g. heparin, heparin sulfate, chondroitin sulfate, keratin sulfate or dermatin sulfate. The receptor is CXCR4 or a CCR5 chemokine receptor. The RL and the RLBM are noncovalently associated prior to admnistration to the patient.

ABEX

ADMINISTRATION - The chemokine and chemokine binding molecule are administered in the form of a rectal or vaginal foam or gel suitable for use as a topical anti-HIV prophylactic agent.

EXAMPLE - Infectivity Assays were carried out with HIV-1. Activated peripheral blood mononuclear cells (PBMC) were infected for 2 hours at 37degreesC with a primary, macrophage tropic HIV-1 isolate, NSI.03, at a ratio of 2x10power6 cells to 500 TCID50 in 5ml culture medium. Cells were then washed to remove virus and placed in tissue culture wells at a density of 2x10power5 cells in 250microl. Complexes were formed by incubating RANTES (5microg/ml final concentration) with 1mg/ml of either heparin, heparan sulfate, chondroitin sulfate or dermatan sulfate for 1 hour at 4degreesC to produce complex formulations containing 641 nM chemokine and 83microM glycosaminoglycan (GAG). The resulting complexes were then serially diluted and 250microl added to culture wells to achieve a total final assay volume of 500microl. Control assays were carried out in parallel with sham formulations containing either RANTES or GAG alone at concentrations equal to the amounts present in the RANTES-GAG complex formulations. The cells were fed 3 days post infection by removing 250microl of medium and replacing with an equal volume of fresh medium containing the appropriate concentrations of RANTES, GAG or RANTES-GAG complexes. Additional control assays were carried out with medium alone. Levels of infection were determined 6 days post-infection by measuring

HIV-1 p24 levels by antigen capture ELISA. The results showed that RANTES-GAG complexes suppressed infection by this isolate. In contrast, sham formulations containing only GAG at the highest concentration (4muM final) used to produce the complexes exhibited lower levels (at most20%) of virus inhibition.

L83 ANSWER 19 OF 41 WPIX (C) 2002 THOMSON DERWENT
AN 1999-610583 [52] WPIX
DNC C1999-177734
TI Nucleic acid delivery vehicles useful for transfecting and infecting a target cell.
DC A96 B04 D16
IN O'RIORDAN, C; ROMANCZUK, H; WADSWORTH, S C; O'RIORDAN, C R
PA (GENZ) GENZYME CORP
CYC 23
PI WO 9940214 A2 19990812 (199952)* EN 118p C12N015-86
RW: AT BE CH CY DE DK ES FI FR GB GR IE IT LU MC NL PT SE
W: AU CA JP US
AU 9926629 A 19990823 (200005)
EP 1053342 A2 20001122 (200061) EN C12N015-86
R: AT BE CH CY DE DK ES FI FR GB GR IE IT LI LU MC NL PT SE
US 6287857 B1 20010911 (200154) C12N015-63
ADT WO 9940214 A2 WO 1999-US2680 19990208; AU 9926629 A AU 1999-26629 19990208; EP 1053342 A2 EP 1999-906805 19990208, WO 1999-US2680 19990208; US 6287857 B1 Provisional US 1998-135092P 19981103, Provisional US 1998-107471P 19981106, CIP of WO 1999-US2680 19990208, US 1999-426680 19991025
FDT AU 9926629 A Based on WO 9940214; EP 1053342 A2 Based on WO 9940214
PRAI US 1998-107471P 19981106; US 1998-20483 19980209; US 1998-135092P 19980209; US 1999-426680 19991025
IC ICM C12N015-63; C12N015-86
ICS **A61K047-48**; A61K048-00; C07H021-04; C12N015-87
AB WO 9940214 A UPAB: 20011012
NOVELTY - A nucleic acid delivery vehicle (I) for transfecting and/or infecting a target cell which comprises a transgene (a) and a bifunctional complex (B) that targets the nucleic acid delivery vehicle to the cell surface, is new.

DETAILED DESCRIPTION - (B) comprises a delivery vehicle binding portion, a cell surface molecule binding portion and a linker connecting them.

An INDEPENDENT CLAIM is also included for a method of delivering a transgene to a target cell comprising contacting the cell with (I) and obtaining expression of the transgene in the target cell.

USE - (I) is used for transfecting and/or infecting a target cell. The delivery vehicle can be specifically targeted to the cell via the binding to cell surface molecules. (I) can be used to target cells, which express integrins such as, HT-29 colon carcinoma cells, lymphocytes and monocytes, blood platelets, SMC-90 human lung fibroblast, MG(63) osteosarcoma cell line, vascular endothelial cells and melanoma cells. (I) is useful for delivery of nucleic acids encoding CFTR (cystic fibrosis transmembrane regulator), - alpha 1-antitrypsin, beta -glucocerebrosidase and suicide genes.

ADVANTAGE - The construct increases the efficiency of cellular uptake of (I). The constructs also enable the transfection/infection of cells that are normally refractory to transfection/infection by targeting cell receptors that are present on such cells.

Dwg.0/19
FS CPI
FA AB; DCN
MC CPI: A12-V01; A12-W11L; **B04-B04C**; B04-C01; B04-C03; B04-E03E; B04-F01; B04-F11; **B04-G01**; B04-H06A; B04-H06G; **B04-H20**; B04-K01; B06-D09; **B14-S03**; D05-C12; D05-H12A; D05-H18

TECH UPTX: 19991210

TECHNOLOGY FOCUS - BIOTECHNOLOGY - Preferred Transgene: (A) is chosen from nucleic acids encoding CFTR, alpha1-antitrypsin, beta-glucocerebrosidase and a suicide gene. The suicide gene is chosen from HSV thymidine kinase, modified thymidine kinase, cystine deaminase, Escherichia colinitroreductase, xanthine-guanine phosphoribosyl transferase, mammalian Pf50 2B1, purine nucleoside phosphorylase, thymidine phosphorylase, deoxycytidine kinase and Varicella Zoster virus thymidine kinase.

Preferred Binding molecule: The cell surface binder binds to a cell surface molecule chosen from receptors, integrins, antigens, molecules with affinity for peptides selected by phage bipanning, negatively charged cell membrane molecules and cell surface enzymes. It is preferably an antibody directed to MHC I, beta2 microglobulin, AF20 antigen, folate receptor, FGF receptor, EGF receptor, c-kit receptor, erythrocyte growth factor receptor, VEGF receptor, polymeric immunoglobulin receptor, purinoreceptor, adenovirus receptor and bFGF receptor. Alternatively it is a ligand, that binds to a cell surface receptor, chosen from folate, transferrin, FGF, EGF, c-kit, erythrocyte growth factor, VEGF and a purine or purine analogue or bFGF. It is preferably a molecule that binds to cell surface integrins, particularly RGD-containing peptides chosen from the following: KGGCRGDMFGCGDGC; KATIRRGDALADGGAC (Bt); KPARGDSSVDGC; KGRARGDNPDGDGC (Viper); KACRGDGWCGDGC; KACPSRLDSPCGDGC; KACDCRGDCFCGDGC; KCDCRGDCFGDGC. The above are cyclic peptides. The Bt peptide is the RGD sequence found in a protein secreted from Bordetella pertusiss called pertactin. The viper sequence is the RGD sequence derived from disintegrin. The remaining peptides are of human origin. The peptides below are linear RGD sequences: GRGDSPC; CRGDCLC; CNRCVSGCAGRC; and CNGRC. Alternatively it is a phage-biopanned peptide whose amino acid sequence is selected from the following: TTDFYYALRALA; LPKMASVQRNLA; HETFYSMIRSLA; HDTFLYGLQRLV; LTFDQTPLTAQI; ITFNQTVTTSYM; ETFSDPLAGSSS (sss.10); SDQLASPYSHPR (sss.17); CGSGSGSGSGSKKKKKKK (p7 poly-lysine peptide); and CGSGSGSGSGSKKKKKKKKKKKKKKKKKKKKK (p21-polylysine peptide) The peptide is especially sss. 10 or sss. 17. Where it binds to a negatively charged cell membrane it is especially p7 or p21-polylysine peptide.

Preferred Linker: The linker may be a small molecule introduced into either (A) or (B), or both, where the small molecule links (B) and (A). The small molecule is a heterofunctional molecule that has both an amine reactive group and a sulfhydryl-reactive group. It is chosen from N-cuccinimidyl 3-(2-pyridyldithio)propionate (SPDP), sccinimidyloxycarbonyl-alpha-methyl-(alpha-2-pyridyldithio)toluene (SMPT), m-maleimidobenzoyl-N-hydroyxsuccinimide ester (MBS), N-succinimidyl(4-iodoacetyl)aminobenzoate (SIAB), succinimyl-4-9p-maleimidophenyl)butyrate (SMPB), N-(gamma-maleimidobutyryloxy)succinimide ester (GMBS), succinimidyl-6-(iodoacetyl)amino)hexanoate) (SIAX), succinimidyl-4(((iodoacetyl)amino)methyl) (SIAC), and p-Nitrophenyl iodoacetate (NPIA). The linker further comprises a sulfo group.

Preferred Delivery Vehicle: (I) is a virus chosen from adenovirus, retrovirus, adeno-associated virus (AAV), herpes simplex virus (HSV) and poxvirus. Where the is an adenovirus (A) binds to the adenovirus. (A) is an antibody or an antibody fragment that binds to hexon or fiber protein. Where (I) is a retrovirus, (A) binds to a retrovirus envelope glycoprotein, e.g. an antibody that binds to gp70. Where the (I) is an AAV, (A) binds to AAV coat protein, e.g. an antibody that binds to VP1, VP2 or VP3. Where (I) is HSV, (A) binds to a surface glycoprotein, e.g. an antibody that binds to gB, gC, gD, gH or gL. Where (I) is a poxvirus, (A) binds to an envelope protein. The (I) is a plasmid of a nucleic acid molecule. (A) is a cationic molecule, e.g. a polycation or cationic lipid. Preferably (I) is a lipid/plasmid complex and (A) is a molecule that binds to the lipid, e.g. an anionic molecule. (A) is chemically reactive with amine groups on the surface of (I) and is an NHS ester or tresyl. Preferably, (I) is an adenovirus and the bifunctional complex comprises a polyethylene glycol polymer having a chemically linked AF20 antibody on

one end and an anti-fiber antibody or an NHS ester/tresyl reactive moiety on the other end. (I) is an adenovirus and the bifunctional complex comprises polyethylene glycol polymer comprising an NHS ester reactive moiety on one end and a vinylsulfone reactive moiety on the other end having a chemically linked sss.17 peptide, polylysine peptide (p7- or p21-polylysine peptides) or bFGF. Alternatively the polyethylene glycol polymer comprises a tresyl reactive moiety on one end and a maleimide reactive moiety on the other end chemically linked sss. 17 peptide, polylysine peptide (p7- or p21-polylysine peptides) or bFGF. TECHNOLOGY FOCUS - POLYMERS - Preferred Linker: The linker is a polyalkalene polymer having an average molecular weight of 200-200000 daltons. The polyalkalene polymer is chosen from polyoxymethylene, polyethylene glycol's, polyethylene oxides, methoxypolyethylene glycol's, polymethyl-ethylene glycol, polyhydroxypropylene glycol, polypropylene glycol, polymethyl propylene glycol and polyhydroxypropylene oxide. The polyalkalene polymer further comprises a chemically reactive moiety at one or both ends. The reactive moiety is chosen from NHS ester, tresyl, maleimide and vinylsulfone. The polyalkalene polymer is polyethylene glycol.

ABEX

WIDER DISCLOSURE - Disclosed as new is a method of producing a delivery construct containing (I).

SPECIFIC PEPTIDES - RGD containing peptidesKGGCRGDMFGCGDGC; KATIRRGDALADGGAC (Bt); KPARGDSSVDGC; KGRARGDNPDGDGC (Viper); KACRGDGWCGDGC; KACPSRLDSPCGDGC; KACDCRGDCFCGDGC; KCDCRGDCFGDGC, linear RGD sequences: GRGDSPC; CRGDCLC; CNRCVSGCAGRC; and CNGRC, and phage-biopanned peptides TTDFYYALRALA; LPKMASVQRNLA; HETFYSMIRSLA; HDTFLYGLQRLV; LTFDQTPLTAQI; ITFNQTVTTSYM; ETFSDPLAGSSS (sss.10); SDQLASPYSHPR (sss.17); CGSGSGSGSGSKKKKKKK (p7 poly-lysine peptide); and CGSGSGSGSGSKKKKKKKKKKKKKKKKKKKK, are given in the specification.

EXAMPLE - Human umbilical vascular endothelial cells (HUVEC) were infected with adenovirus (Ad2beta-gal4) in the presence of increasing amounts of a bifunctional Fab complex. Increasing the amount of bifunctional Fab led to a corresponding increase in infection of HUVEC cells suggesting that the bifunctional complex could mediate adenoviral infectivity in these cells. Expression of the transgene (beta-galactosidase) in HUVEC cells infected with Ad2-beta-bgal4 vector in the presence of a reactive bifunctional Fab complex was compared with the expression in HUVEC cells infected with Ad2-Bgal4 vector in the presence of a non-reactive bifunctional complex. The reactive bifunctional Fab complex was shown to recognize both hexon and b2-microglobulin in an ELISA format, while the non-reactive complex failed to recognize hexon in the ELISA. There was a significant increase in transgene expression (up to 4-fold over expression measured with the Ad2-bgal-4 vector alone) in HUVEC cells infected with vector in the presence of the targeting complex.

L83 ANSWER 20 OF 41 WPIX (C) 2002 THOMSON DERWENT
AN 1999-468944 [39] WPIX
DNC C1999-137535
TI Solid nanospheres for genetic immunization of mammals, to raise immune response to antigen by cell-mediated and humoral immune responses.
DC A96 B04 D16
IN AUGUST, J T; LEONG, K W; TRUONG, V
PA (UYJO) UNIV JOHNS HOPKINS
CYC 85
PI WO 9936089 A1 19990722 (199939)* EN 33p A61K039-39 <--
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW NL OA PT SD SE SZ UG ZW
W: AL AM AT AU AZ BA BB BG BR BY CA CH CN CU CZ DE DK EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT

UA UG US UZ VN YU ZW
AU 9921172 A 19990802 (199954) A61K039-39 <--
EP 1045699 A1 20001025 (200055) EN A61K039-39 <--
R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT RO SE SI
AU 743226 B 20020124 (200221) A61K039-39 <--
JP 2002509116 W 20020326 (200236) 33p A61K048-00

ADT WO 9936089 A1 WO 1999-US860 19990115; AU 9921172 A AU 1999-21172 19990115; EP 1045699 A1 EP 1999-901486 19990115, WO 1999-US860 19990115; AU 743226 B AU 1999-21172 19990115; JP 2002509116 W WO 1999-US860 19990115, JP 2000-539862 19990115

FDT AU 9921172 A Based on WO 9936089; EP 1045699 A1 Based on WO 9936089; AU 743226 B Previous Publ. AU 9921172, Based on WO 9936089; JP 2002509116 W Based on WO 9936089

PRAI US 1998-71746P 19980116

IC ICM **A61K039-39**; A61K048-00
ICS **A61K009-51**; A61K031-711; A61K038-00; **A61K047-36**; **A61K047-42**; **A61K047-48**

AB WO 9936089 A UPAB: 19990928

NOVELTY - New solid nanospheres of less than 5 mu m for genetic immunization of mammals comprising coacervate of polymeric cation and polyanion of nucleic acids, where at least a portion of the nucleic acids encode an antigen, and where a cytokine is encapsulated in coacervate.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following:

(1) A method of immunizing a mammal to raise an immune response to an antigen comprising administering to a mammal a solid nanosphere as defined above; and

(2) a method of forming solid nanospheres for immunization of a mammal, comprising forming solid nanospheres by coacervation of a polyanion consisting of nucleic acids encoding an antigen and a polymeric cation, where the coacervation is done in the presence of a cytokine which is encapsulated in the solid spheres.

ACTIVITY - Antiviral; antibacterial; anti-tumor.

BALB/c mice (8 weeks) were divided into groups of 10. The mice were immunized by intramuscular injection in the tibialis anterior with three monthly injections of nanospheres containing 0.5 or 3 mu g nanosphere DNA encoding Ebola nucleoprotein (NP); 0.5 or 3 mu g nanosphere DNA encoding Ebola envelope glycoprotein (GP) antigens or 3 mu g control WRG7077 pDNA (vector without the Ebola NP or GP insert). The mice then were challenged with 30 multiply LD50 of mouse-adapted live Ebola Zaire strain. Survival rates were tabulated at week 12. No deaths were observed after day 10. The survival rate was better with each antigen than with vector control and was significantly greater with the higher dose (p less than 0.05). A higher degree of protection was achieved with Ebola NP vaccination than with Ebola GP (90% versus 40%). The geometric means anti-GP or anti-NP antibody titers of immunized mice were low, 1 plus or minus 0.1 multiply 102. Vaccination with DNA nanospheres was at least as efficient as the gene gun vaccination method. The results suggested that the nanosphere may provide an important new type of DNA vaccine delivery system of particular value in disease states in which a specific immune response phenotype is required. A parallel challenge experiment using the NP antigen given as PowerJect-XR (gene gun) gene gun DNA (3 mu g dose, three total vaccinations) showed a protection level of 80%.

MECHANISM OF ACTION - Cell mediated response stimulation; humoral immune response stimulation.

USE - The nanospheres are used to immunize mammals to raise immune response to antigen (claimed) by cell-mediated and humoral immune responses. They are also used to deliver genes encoding antigens to mammals, to target parenchymal cells of the liver sinusoids, fibroblasts of the connective tissues, cells in the Islets of Langerhans in the pancreas, cardiac myocytes, Chief and parietal cells of the intestine, osteocytes and chondrocytes in bone, keratinocytes, nerve cells of the

peripheral nervous system, epithelial cells of the kidney and lung, Sertoli cells of the testis, erythrocytes, leukocytes (monocytes, macrophages, B and T lymphocytes, neutrophils, natural killer cells, progenitor cells, mast cells, eosinophils), platelets and endothelial cells. The nanospheres are used to immunize against HIV and Ebola infections.

ADVANTAGE - The nanosphere provides non-viral gene delivery system for delivery of nucleic acids for immunization of animals. Temporal and spatial distribution of cytokines can be altered, thus directing immune response towards a specific immune arm, for example allowing modulating immune response against HIV infection by emphasizing humoral or cellular arm. Coacervate is extracellularly stable. Ligands can be conjugated to nanospheres to stimulate receptor-mediated endocytosis and potentially to target cells/tissues. Lysosomolytic agents can be incorporated to promote escape of intact DNA into cytoplasm. Other bioactive agents (RNA, oligonucleotides, proteins or multiple plasmids) can be co-encapsulated for potential augmentation of immune response through class I presentation. Bioavailability of nucleic acids is improved because of protection from serum nuclease degradation by the matrix and there is little release of nucleic acids until the nanosphere is sequestered into the endolysosomal pathway. There is potential of intracellular sustained release of nucleic acids that may provide more prolonged expression of gene product. Nanosphere is stable in plasma electrolytes and can be lyophilized without loss of bioactivity. Nanospheres can be handled like conventional pharmaceutical formulations in terms of production, reproducibility and storage.

DESCRIPTION OF DRAWING(S) - Survival of mice infected with Ebola virus following vaccination with Ebola nucleoprotein (NP) pDNA or Ebola envelope glycoprotein (GP) pDNA delivered by nanosphere. Open square = 0.5 mu g Ebola NP pDNA; filled square = 3 mu g Ebola NP pDNA; open circle = 0.5 mu g Ebola GP pDNA; filled circle = 3 mu g Ebola GP pDNA; open triangle = 3 mu g control WRG7077 pDNA (vector without the Ebola NP or GP insert).

5A, 5B/5

FS CPI

FA AB; GI; DCN

MC CPI: A12-V01; B04-C02E3; B04-E02B; B04-F02; **B04-G01**; B04-H02; B04-H04; B04-J01; B04-N02; B14-A01; B14-A02B1; **B14-H01**; D05-H10; D05-H11; D05-H12A

TECH UPTX: 19990928

TECHNOLOGY FOCUS - ORGANIC CHEMISTRY - Preferred Nanospheres - Polymeric cation is gelatin or chitosan. Cell-targeting ligand is attached to the nanospheres, preferably covalently through glutaraldehyde cross-linking.

TECHNOLOGY FOCUS - BIOTECHNOLOGY - Preferred Nucleic Acids - At least a portion of the nucleic acids encodes a cytokine, preferably granulocyte-macrophage colony-stimulating factor (GM-CSF), tumor necrosis factor alpha (TNF-alpha), interleukin (IL) 12, IL-4 and/or gamma-interferon (gamma-IFN). Nucleic acids encode a gene of 2-10 kb. Preferred antigen - The antigen is a viral, bacterial or tumor-associated antigen. The antigen is also encapsulated in the coacervate. Preferred Method: The method of (2) also comprises cross-linking a cell targeting ligand to the nanospheres. Coacervation is performed in the presence of sodium sulfate. The targeting ligand is antibodies, hormones, **cell adhesion molecules**, saccharides, drugs or neurotransmitters. Gelatin is present at a concentration of 2-7% in the step of coacervation. The nucleic acids are present in a concentration of 1 ng/ml to 500 microg/ml and the sodium sulfate is between 7 and 43 mM in the step of coacervation.

ABEX

ADMINISTRATION - Administration is by injection into muscle, by subcutaneous injection or by bombardment with nanospheres from a high-pressure gene gun (claimed) as well as by intravenous,

intra-arterial, intra-peritoneal or intrathecal injection.

EXAMPLE - No relevant example given.

L83 ANSWER 21 OF 41 WPIX (C) 2002 THOMSON DERWENT
AN 1999-444321 [37] WPIX
DNC C1999-130892
TI A patient-specific vaccine for treating white blood cell malignancies.
DC B04 B05 D16
IN BATENJANY, M M; BONI, L; POPESCU, M C; ROBB, R J
PA (BIOM-N) BIOMIRA USA INC; (BATE-I) BATENJANY M M; (BONI-I) BONI L; (POPE-I) POPESCU M C; (ROBB-I) ROBB R J
CYC 85
PI WO 9936085 A1 19990722 (199937)* EN 22p A61K039-00 <--
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW NL OA PT SD SE SZ UG ZW
W: AL AM AT AU AZ BA BB BG BR BY CA CH CN CU CZ DE DK EE ES FI GB GD GE GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT UA UG US UZ VN YU ZW
AU 9920318 A 19990802 (199954) A61K039-00 <--
EP 1045698 A1 20001025 (200055) EN A61K039-00 <--
R: AT BE CH CY DE DK ES FI FR GB GR IE IT LI LU MC NL PT SE
US 6207170 B1 20010327 (200119) A61K039-00 <--
US 2001012517 A1 20010809 (200147) A61K039-00 <--
AU 737330 B 20010816 (200153) A61K039-00 <--
JP 2002509114 W 20020326 (200236) 23p A61K039-00 <--
ADT WO 9936085 A1 WO 1999-US935 19990115; AU 9920318 A AU 1999-20318 19990115; EP 1045698 A1 EP 1999-900822 19990115, WO 1999-US935 19990115; US 6207170 B1 Provisional US 1998-71702P 19980116, US 1999-231650 19990115; US 2001012517 A1 Provisional US 1998-71702P 19980116, Cont of US 1999-231650 19990115, US 2001-816266 20010326; AU 737330 B AU 1999-20318 19990115; JP 2002509114 W WO 1999-US935 19990115, JP 2000-539858 19990115
FDT AU 9920318 A Based on WO 9936085; EP 1045698 A1 Based on WO 9936085; US 2001012517 A1 Cont of US 6207170; AU 737330 B Previous Publ. AU 9920318, Based on WO 9936085; JP 2002509114 W Based on WO 9936085
PRAI US 1998-71702P 19980116; US 1999-231650 19990115; US 2001-816266 20010326
IC ICM **A61K039-00**
ICS **A61K009-127**; **A61K039-385**; **A61K039-39**; **A61K047-00**; **A61K047-02**; A61P035-02
AB WO 9936085 A UPAB: 20011203
NOVELTY - A patient-specific vaccine for treating white blood cell (WBC) malignancy, comprising a membrane-proteoliposome (MP) containing plasma membrane from a malignant white blood cell, is new.
DETAILED DESCRIPTION - An INDEPENDENT CLAIM is also included for a membrane-proteoliposome (MP), comprising integral membrane from a malignant WBC, at least one immuno-stimulator and an exogenous lipid.
ACTIVITY - Cytostatic.
MECHANISM OF ACTION - Vaccine.
USE - The vaccine can be used to treat lymphoma, leukemia and myeloma (all claimed).
ADVANTAGE - The vaccine is developed on the patient's own WBCs, so the vaccine is highly specific.
Dwg.0/2
FS CPI
FA AB; DCN
MC CPI: B04-B01B; B04-H02; B04-H04B; B04-H04C; B04-H05; B05-B01P; **B14-H01A**; B14-S11C; D05-H07
TECH UPTX: 19990914
TECHNOLOGY FOCUS - PHARMACEUTICALS - Preferred Vaccine: The WBC is a lymphoma cell, a leukemia cell or a myeloma cell. The membrane contains at least one membrane component involved in immunity. MP comprises at least

two immunostimulators. The component is selected from tumor-specific antigen, a major histocompatability complex antigen and a co-stimulatory molecule, especially B7.1, B7.2 or **ICAM-1**. The immunostimulator is a lymphokine, especially interleukin (IL)-2, interferon (especially IFN-7), cytokine (such as granulocyte macrophage colony stimulating factor (GM-CSF) or macrophage colony stimulating factor (M-CSF) or adjuvant selected from monophosphoryl lipid A, lipid A and muramyl dipeptide (MDP) lipid conjugate. The lipid is a saturated or unsaturated phospholipid or a glycolipid, selected from 1,2-dimyristoylphosphatidylcholine, 1,2-dipalmitoylphosphatidylcholine, 1,2-dimyristoylphosphatidylglycerol and/or cholesterol. The lipid forms a membrane within which the integral membrane is patched or the lipid forms patches within the integral membrane.

ABEX

EXAMPLE - Experimental vaccine MB-RM-IA was formulated as follows: 1,2-dimyristoylphosphatidylcholine (DMPC) powder (1g), 4 ml of the isolated 38C13 membranes (225 mug/mL IgM) in normal saline solution (NSS) and 160 microlitre of interleukin 2 (IL-2) (1.25x108 IU/ml) were placed in a 5 ml sterile glass vial, immediately vortexed, heated to 37 degrees Centigrade for 15 minutes in a water bath, then sonicated at 37 degrees Centigrade for 30 seconds in a bath sonicator. This suspension was subjected to three freeze/thaw cycles as follows:
(a) freezing at -70 degrees Centigrade (dry ice/methanol bath) for 15 minutes;
(b) thawing at 37 degrees Centigrade (water bath) for 15 minutes;
(c) vortexing briefly; and
(d) sonicating for 30 seconds in a bath sonicator at 37 degrees Centigrade.
The preparation was adjusted to a total volume of 5 ml with NSS and stored at -70 degrees Centigrade.

L83 ANSWER 22 OF 41 WPIX (C) 2002 THOMSON DERWENT
AN 1997-087383 [08] WPIX
DNC C1997-028484
TI New antibody specific for new 85 kD adhesion protein on endothelial or muscle cells - and related nucleic acid, recombinant cells etc., for inhibiting tumour metastasis and leucocyte adhesion to endothelial cells induced by ischaemia or hypoxia.
DC B04 D16
IN FALLER, D V; GINIS, I; MENTZER, S J
PA (UYBO-N) UNIV BOSTON
CYC 70
PI WO 9700956 A1 19970109 (199708)* EN 53p C12N015-12
RW: AT BE CH DE DK EA ES FI FR GB GR IE IT KE LS LU MC MW NL OA PT SD SE SZ UG
W: AL AM AT AU AZ BB BG BR BY CA CH CN CZ DE DK EE ES FI GB GE HU IL IS JP KE KG KP KR KZ LK LR LS LT LU LV MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK TJ TM TR TT UA UG UZ VN
AU 9663906 A 19970122 (199719) C12N015-12
ADT WO 9700956 A1 WO 1996-US10701 19960620; AU 9663906 A AU 1996-63906 19960620
FDT AU 9663906 A Based on WO 9700956
PRAI US 1995-493053 19950620
REP 8.Jnl.Ref; WO 9003400; WO 9116928; WO 9319784; WO 9425067
IC ICM C12N015-12
ICS A61K038-17; **A61K039-395**; **A61K047-48**; A61K051-10; C07K016-28; C07K016-30; C12N005-10; C12N005-20
AB WO 9700956 A UPAB: 19970220
Antibody (Ab), or fragments, that bind specifically to a **cell adhesion molecule** (I), derived from human endothelial or muscle cells and of mol. wt. about 85 kD, is new. Also new are: (1) hybridomas that express Ab; (2) purified or recombinant (I); (3) ligands (II) having a binding site for (I); (4) purified nucleic acid (III)

encoding (I); and (5) recombinant cells contg. (III).

Ab may be poly- or mono-clonal, and is human, humanised or (partly) murine of IgG1-4, IgM, IgA1-2, IgD and/or IgE class, pref. IgG1, IgG2a, IgG2b, IgM, IgA, IgD and/or IgE, pref. IgG1, IgG2a, IgG2b, IgM, IgA, IgD or IgE. The fragments are pref. Fab and Fv. Ab may be coupled to e.g. (a) a toxin of animal or plant origin, esp. Pseudomonas, Diphtheria or Escherichia toxins or ricin or (2) a radioisotope, ribozyme, antisense nucleic acid and/or a pharmaceutical agent. It may be administered together with a chemotherapeutic agent, e.g. alkylating agent, purine or pyrimidine deriv., etc. Ab is specifically HAL 1/13, expressed by hybridoma ATCC HB 11979. (I) is derived from endothelial, muscle, neural, neuroblastoma, breast cancer or other tumour cells. (III) is expressed in prokaryotic or eukaryotic cells; specified are ATCC 69852 and 69853 (E. coli XL1 Blue expressing (I)). (II) may be a protein, lipid and/or saccharide having a binding site for (I).

USE - Ab inhibit (1) metastasis of neoplastic cells (they may prevent colonisation or kill neoplastic cells), i.e. leukaemia, lymphoma, sarcoma, (squamous cell) carcinoma, neural or germ cell tumours, undifferentiated tumours, seminoma, melanoma, neuroblastoma, mixed cell tumour, neoplasia caused by infection and other malignancies and (2) ischaemia- or hypoxia-induced adhesion of leucocytes to endothelial cells (e.g. for treatment of coronary thrombosis, cerebral vascular disease, arteriosclerosis, fibrosis, angiogenesis, tumour formation, plaque formation in blood vessels, and inflammation; to minimise damage to tissue caused by stroke or myocardial infarction, and to inhibit anaphylaxis or other allergic responses). (I) can be used in vaccines to prevent similar conditions. Ab are also useful for imaging metastatic spread. Ab are administered by intravenous, subcutaneous, intramuscular or intra-arterial injection for inhibition of leucocyte adhesion, also directly into the tumour for control of metastases. No dose is given.

Dwg.9/9

FS CPI

FA AB; GI

MC CPI: B04-A07A; B04-E03F; B04-F0100E; B04-F05; B04-F10A3E; **B04-G01** ; B04-G21; B04-G22; B04-J02; B04-N01; B04-N02; B04-N03; B05-A03B; B12-K04A; B14-C03; B14-D02; B14-F01E; B14-F02D; B14-F04; B14-F07; **B14-H01B**; B14-N16; B14-S11C; D05-H09; D05-H11A1; D05-H12A; D05-H14; D05-H15

L83 ANSWER 23 OF 41 WPIX (C) 2002 THOMSON DERWENT

AN 1997-065170 [06] WPIX

DNC C1997-021404

TI New carbamate based cationic lipid(s) for cellular delivery of polyanions, esp. expression vectors, anti sense nucleic acids etc. - are more effective than known lipids and can transfect wide range of cells over broad confluency range.

DC B01 B04 B05 B07 D16

IN BROWN, B D; DWYER, B P; SCHWARTZ, D A

PA (GENT-N) GENTA INC

CYC 23

PI WO 9640726 A1 19961219 (199706)* EN 75p C07J009-00
RW: AT BE CH DE DK ES FI FR GB GR IE IT LU MC NL PT SE
W: AU CA JP KR NZ
AU 9661617 A 19961230 (199716) C07J009-00
EP 830368 A1 19980325 (199816) EN C07J009-00
R: AT BE CH DE DK ES FI FR GB GR IE IT LI LU MC NL PT SE
AU 701106 B 19990121 (199915) C07J009-00
JP 11507352 W 19990629 (199936) 57p C07J009-00

ADT WO 9640726 A1 WO 1996-US9553 19960605; AU 9661617 A AU 1996-61617 19960605; EP 830368 A1 EP 1996-919222 19960605, WO 1996-US9553 19960605; AU 701106 B AU 1996-61617 19960605; JP 11507352 W WO 1996-US9553 19960605, JP 1997-501850 19960605

FDT AU 9661617 A Based on WO 9640726; EP 830368 A1 Based on WO 9640726; AU

701106 B Previous Publ. AU 9661617, Based on WO 9640726; JP 11507352 W Based on WO 9640726
PRAI US 1995-483465 19950607
REP 1.Jnl.Ref; US 4680290; US 4897355; US 5171678; US 5283185; US 5334761
IC ICM C07J009-00
ICS **A61K009-127**; A61K038-00; C07C269-00; C07C271-20; C07D233-61
AB WO 9640726 A UPAB: 19970205
Lipids of formula R2-(CH2)n-NH-CO-OR1 (X-)m (I) and their salts, solvates and enantiomers are new, in which R1 = a lipophilic gp., R2 = a positively charged gp., X = an anion or polyanion, n = 1-8, and m = 0 to the number of positive charges in (I). Also new are the intermediates N-(18-pentatriacontyloxycarbonyl)-2-aminoethanol (II) and carboxyspermyl-N-(18-pentatriacontyloxycarbonyl)ethylene diamine (III). Also claimed is a compsn. contg. (I) and a polyanionic macromolecule (IV).

USE - (I) are used to deliver (IV), e.g. expression vectors, oligonucleotides, oligomers or DNA, to cells, in vitro or in vivo, partic. for delivery of antisense oligonucleotides to inhibit expression of a particular protein, e.g. to inhibit proteases (thus increasing yield of target protein) or to inhibit antigen synthesis to prevent rejection and/or induce immunogenic tolerance to transplanted cells. They can also be used to deliver sequences encoding therapeutic or diagnostic polypeptides, e.g. histocompatibility antigens, adhesion molecules, cytokines, antibodies etc., for therapeutic use (including vaccination) or for mfr. of proteins such as enzymes, growth factors etc.

ADVANTAGE - (I) improves cellular uptake of (IV) even in presence of serum, and is 2-100 times more effective than commercially available transfection lipids. Also (I) can transfect some cells which are resistant to conventional methods, and they are active over a broad range of cell confluence (50-100%).

Dwg.0/6
FS CPI
FA AB; DCN
MC CPI: B04-B03C; B04-E01; B04-E06; B04-E08; **B04-G01**; B04-H01; **B04-H20**; B05-B01P; B10-A12C; B14-D07C; B14-G02C; D05-H07; D05-H08; D05-H09; D05-H12D2; D05-H12E

L83 ANSWER 24 OF 41 WPIX (C) 2002 THOMSON DERWENT
AN 1997-051818 [05] WPIX
DNC C1997-017096
TI System for forming drug-loaded microparticles for sustained drug release - involves mixing soln. contg. drug and microparticle-forming polymer with emulsifier and crosslinking agent.
DC A96 B07
IN BOMBERGER, D C; CATZ, P G; SMEDLEY, M I; STEARNS, P C
PA (STRI) SRI INT
CYC 21
PI WO 9640069 A1 19961219 (199705)* EN 44p A61K009-14 <--
RW: AT BE CH DE DK ES FI FR GB GR IE IT LU MC NL PT SE
W: CA JP
EP 833614 A1 19980408 (199818) EN A61K009-14 <--
R: AT BE CH DE DK ES FI FR GB GR IE IT LI LU MC NL PT SE
US 5879712 A 19990309 (199917) A61K009-14 <--
JP 11507382 W 19990629 (199936) 41p A61K009-14 <--
US 6375985 B1 20020423 (200232) A61K009-14 <--
ADT WO 9640069 A1 WO 1996-US10031 19960606; EP 833614 A1 EP 1996-918456 19960606, WO 1996-US10031 19960606; US 5879712 A US 1995-480624 19950607; JP 11507382 W WO 1996-US10031 19960606, JP 1997-502167 19960606; US 6375985 B1 Div ex US 1995-480624 19950607, US 1999-583089 19990308
FDT EP 833614 A1 Based on WO 9640069; JP 11507382 W Based on WO 9640069; US 6375985 B1 Div ex US 5879712
PRAI US 1995-480624 19950607; US 1999-583089 19990308
REP US 5476663
IC ICM **A61K009-14**

ICS **A61K009-50; A61K009-66;** A61K038-00; **A61K039-00**

AB WO 9640069 A UPAB: 19970129

A system for forming microparticles loaded with a drug comprises: (A) a first mixing chamber, including a 1st port for introducing a 1st stream of a 1st soln. comprising a predetermined amt. of the drug and microparticle-forming polymer into 1st mixing chamber; and a second port for introducing a 2nd stream of an emulsifier into the 1st stream, to form an emulsion in the 1st mixing chamber; and (B) a 2nd mixing chamber, adjacent to the 1st, including a third port for introducing a crosslinking soln. contg. a predetermined amt. of a crosslinking agent in a crosslinking solvent, into the 2nd mixing chamber.

Also claimed are (1) an **intercellular adhesion molecule ICAM-1** compsn. consisting of: (A) **intercellular adhesion molecule ICAM -1**, one or more functional domains of **ICAM-1** , one or more biologically active **ICAM-1** fragments or their analogues, or combinations and functional derivs.; and (B) crosslinked alginate; and (2) microparticles of dia. < 100mum, contg. (A) **intercellular adhesion molecule ICAM -1**, its functional domains, biologically active fragments or analogues, or combinations and functional derivs.; and (B) non-starch polymer.

USE - **Intercellular adhesion molecule ICAM-1** is used in a pharmaceutical formulation to complex with rhinovirus and rhinovirus binding to human nasal membranes. It is used in the mfr. of medicaments.

Dwg.0/4

FS CPI

FA AB; DCN

MC CPI: A03-A00A; A12-V01; B04-C02D; B05-A01B; B10-C04E; B10-E04D; B10-J02; B12-M11E

L83 ANSWER 25 OF 41 WPIX (C) 2002 THOMSON DERWENT

AN 1996-497572 [49] WPIX

DNC C1996-155554

TI New anti-inter-**cellular adhesion mol.**-I antibodies - deriv. with polyethylene glycol to reduce immunogenicity and increase in vivo serum half-life.

DC A25 A96 B04 D16

IN FAANES, R B; MCGOFF, P E; SCHER, D S; SHIRLEY, B A

PA (BOEH) BOEHRINGER INGELHEIM PHARM INC

CYC 74

PI WO 9634015 A1 19961031 (199649)* EN 104p C07K016-28

RW: AT BE CH DE DK EA ES FI FR GB GR IE IT KE LS LU MC MW NL OA PT SD SE SZ UG

W: AL AM AT AU AZ BB BG BR BY CA CH CN CZ DE DK EE ES FI GB GE HU IS JP KE KG KP KR KZ LK LR LS LT LU LV MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK TJ TM TR TT UA UG US UZ VN

ZA 9603287 A 19961030 (199649) 104p C07K000-00

AU 9655633 A 19961118 (199710) C07K016-28

US 5695760 A 19971209 (199804) 26p A61K039-395 <--

EP 822942 A1 19980211 (199811) EN C07K016-28

R: AT BE CH DE DK ES FI FR GB GR IE IT LI LU MC NL PT SE

JP 11504516 W 19990427 (199927) 102p C12N015-02

IL 117993 A 20000831 (200052) C07K016-28

TW 438809 A 20010607 (200175) A61K039-44 <--

ADT WO 9634015 A1 WO 1996-US5550 19960423; ZA 9603287 A ZA 1996-3287 19960424; AU 9655633 A AU 1996-55633 19960423; US 5695760 A US 1995-427355 19950424; EP 822942 A1 EP 1996-912995 19960423, WO 1996-US5550 19960423; JP 11504516 W JP 1996-532624 19960423, WO 1996-US5550 19960423; IL 117993 A IL 1996-117993 19960421; TW 438809 A TW 1996-110360 19960826

FDT AU 9655633 A Based on WO 9634015; EP 822942 A1 Based on WO 9634015; JP

11504516 W Based on WO 9634015
PRAI US 1995-427355 19950424
REP 8.Jnl.Ref; WO 8604145; WO 9116927; WO 9204034; WO 9317047
IC ICM **A61K039-395**; **A61K039-44**; C07K000-00; C07K016-28; C12N015-02
ICS **A61K047-48**; A61P029-00; A61P031-12; A61P037-00; C07K001-20; C07K016-00; C07K016-20; C07K017-08; C12P021-08
AB WO 9634015 A UPAB: 19961205
A polyethylene glycol (PEG)-modified deriv. of an anti-**intercellular adhesion mol.-1** (**ICAM-1**) antibody, where the antibody is capable of binding to **ICAM-1**, and of inhibiting **ICAM-1**-mediated cellular adhesion.

Also claimed is a method of purifying a PEG-modified antibody species from a prepn. contg. the species and a non-modified species of the antibody, which comprises subjecting the prepn. to hydrophobic interaction chromatography (HIC) under conditions sufficient to separate the non-modified species of the antibody from the PEG-modified species and recovering the sepd. PEG-modified antibody.

USE - The PEG-modified anti-**ICAM-1** antibodies can be used for treating or preventing inflammation caused by autoimmune disease, asthma, adult respiratory distress syndrome, multiple organ injury syndromes secondary to septicaemia or trauma, reperfusion injury, acute glomerulonephritis, reactive arthritis, dermatoses with acute inflammatory components, acute purulent meningitis, central nervous system inflammatory disorders, thermal injury, haemodialysis, leukapheresis, ulcerative colitis, Crohn's disease, necrotising enterocolitis, granulocyte transfusion associated syndromes and cytokine-induced toxicity. They can also be used for treating or preventing rhinovirus infection (all claimed).

ADVANTAGE - The PEG-modified anti-**ICAM-1** antibodies exhibit reduced immunoreactivity in vivo compared to unmodified antibodies, while retaining the ability to inhibit cellular adhesion. In addn., the modified antibodies have a longer in vivo serum half life.

Dwg.0/5
FS CPI
FA AB; DCN
MC CPI: A10-E01; A12-V01; B04-C03C; **B04-G01**; B14-A01; B14-A02B7; B14-C03; B14-C09; B14-F05; B14-G02D; **B14-H01A**; B14-K01A; B14-K01D; B14-N10; B14-N16; B14-N17C; B14-S06; B14-S07; D05-H11A
ABEQ US 5695760 A UPAB: 19980126
A polyethylene glycol (PEG)-modified deriv. of an anti-**intercellular adhesion mol.-1** (**ICAM-1**) antibody, where the antibody is capable of binding to **ICAM-1**, and of inhibiting **ICAM-1**-mediated cellular adhesion.

Also claimed is a method of purifying a PEG-modified antibody species from a prepn. contg. the species and a non-modified species of the antibody, which comprises subjecting the prepn. to hydrophobic interaction chromatography (HIC) under conditions sufficient to separate the non-modified species of the antibody from the PEG-modified species and recovering the sepd. PEG-modified antibody.

USE - The PEG-modified anti-**ICAM-1** antibodies can be used for treating or preventing inflammation caused by autoimmune disease, asthma, adult respiratory distress syndrome, multiple organ injury syndromes secondary to septicaemia or trauma, reperfusion injury, acute glomerulonephritis, reactive arthritis, dermatoses with acute inflammatory components, acute purulent meningitis, central nervous system inflammatory disorders, thermal injury, haemodialysis, leukapheresis, ulcerative colitis, Crohn's disease, necrotising enterocolitis, granulocyte transfusion associated syndromes and cytokine-induced toxicity. They can also be used for treating or preventing rhinovirus infection (all claimed).

ADVANTAGE - The PEG-modified anti-**ICAM-1** antibodies exhibit reduced immunoreactivity in vivo compared to unmodified antibodies, while retaining the ability to inhibit cellular adhesion. In addn., the modified antibodies have a longer in vivo serum half life. Dwg.0/0

L83 ANSWER 26 OF 41 WPIX (C) 2002 THOMSON DERWENT
AN 1996-171367 [17] WPIX
CR 1995-058869 [08]
DNC C1996-054022
TI Substantially water-insoluble metal salt of physiologically active peptide, e.g. enzyme, antibody - in sustained release compsn. contg. a biodegradable polymer, prepd. by dispersing salt in oil phase, then adding to water phase.
DC A96 B04 B07
IN IGARI, Y; IINUMA, S; OKADA, H; YAMAGATA, Y; IKEDA, H; TSUDA, M; WAKIMASU, M; YAMAMOTO, K
PA (TAKE) TAKEDA CHEM IND LTD; (TAKE) TAKEDA YAKUHIN KOGYO KK; (IGAR-I) IGARI Y; (IINU-I) IINUMA S; (IKED-I) IKEDA H; (OKAD-I) OKADA H; (TSUD-I) TSUDA M; (WAKI-I) WAKIMASU M; (YAMA-I) YAMAGATA Y; (YAMA-I) YAMAMOTO K
CYC 65
PI WO 9607399 A1 19960314 (199617)* EN 37p A61K009-16 <--
RW: AT BE CH DE DK ES FR GB GR IE IT KE LU MC MW NL OA PT SD SE SZ UG
W: AM AU BB BG BR BY CA CN CZ EE FI GE HU IS KG KR KZ LK LR LT LV MD MG MK MN MX NO NZ PL RO RU SG SI SK TJ TM TT UA US UZ VN
AU 9533990 A 19960327 (199627)
JP 08217691 A 19960827 (199644) 11p A61K038-00
FI 9700952 A 19970306 (199723) A61K000-00
NO 9701030 A 19970306 (199724) A61K009-16 <--
EP 779806 A1 19970625 (199730) EN
R: AT BE CH DE DK ES FR GB GR IE IT LI LU NL PT SE
BR 9509201 A 19971230 (199807)
KR 97705379 A 19971009 (199841)
AU 695323 B 19980813 (199844)
NZ 292263 A 19981223 (199906)
EP 1002529 A1 20000524 (200030) EN A61K009-16 <--
R: AT BE CH DE DK ES FR GB GR IE IT LI LT LU LV MC NL PT SE SI
US 6087324 A 20000711 (200040) A61K028-18
EP 779806 B1 20001108 (200062) EN A61K009-16 <--
R: AT BE CH DE DK ES FR GB GR IE IT LI LU NL PT SE
DE 69519382 E 20001214 (200104) A61K009-16 <--
ES 2151079 T3 20001216 (200105) A61K009-16 <--
CN 1157562 A 19970820 (200137) A61K009-16 <--
US 6376461 B1 20020423 (200235) A01N037-18
US 2002058622 A1 20020516 (200239) A61K038-22
RU 2181999 C2 20020510 (200248) A61K009-52 <--
ADT WO 9607399 A1 WO 1995-JP1771 19950906; AU 9533990 A AU 1995-33990 19950906; JP 08217691 A JP 1995-230841 19950908; FI 9700952 A WO 1995-JP1771 19950906, FI 1997-952 19970306; NO 9701030 A WO 1995-JP1771 19950906, NO 1997-1030 19970306; EP 779806 A1 EP 1995-930707 19950906, WO 1995-JP1771 19950906; BR 9509201 A BR 1995-9201 19950906, WO 1995-JP1771 19950906; KR 97705379 A WO 1995-JP1771 19950906, KR 1997-701548 19970308; AU 695323 B AU 1995-33990 19950906; NZ 292263 A NZ 1995-292263 19950906, WO 1995-JP1771 19950906; EP 1002529 A1 Div ex EP 1995-930707 19950906, EP 1999-203867 19950906; US 6087324 A CIP of US 1994-265124 19940624, CIP of WO 1995-JP1771 19950906, US 1996-644631 19960422; EP 779806 B1 EP 1995-930707 19950906, WO 1995-JP1771 19950906, Related to EP 1999-203867 19950906; DE 69519382 E DE 1995-619382 19950906, EP 1995-930707 19950906, WO 1995-JP1771 19950906; ES 2151079 T3 EP 1995-930707 19950906; CN 1157562 A CN 1995-194963 19950906; US 6376461 B1 CIP of US 1994-265124 19940624, CIP of WO 1995-JP1771 19950906, Cont of US 1996-644631 19960422, US 1999-426716 19991026; US 2002058622 A1 CIP of US 1994-265124 19940624, CIP of WO 1995-JP1771 19950906, Cont of US 1996-644631 19960422, Div ex US

1999-426716 19991026, US 2001-985925 20011106; RU 2181999 C2 WO 1995-JP1771 19950906, RU 1997-105827 19950906

FDT AU 9533990 A Based on WO 9607399; EP 779806 A1 Based on WO 9607399; BR 9509201 A Based on WO 9607399; KR 97705379 A Based on WO 9607399; AU 695323 B Previous Publ. AU 9533990, Based on WO 9607399; NZ 292263 A Based on WO 9607399; EP 1002529 A1 Div ex EP 779806; EP 779806 B1 Related to EP 1002529, Based on WO 9607399; DE 69519382 E Based on EP 779806, Based on WO 9607399; ES 2151079 T3 Based on EP 779806; US 6376461 B1 Cont of US 6087324; US 2002058622 A1 Cont of US 6087324; RU 2181999 C2 Based on WO 9607399

PRAI JP 1994-310291 19941214; JP 1994-216449 19940909; JP 1993-153393 19930624

REP WO 9317668; WO 9412158

IC ICM A01N037-18; A61K000-00; **A61K009-16**; **A61K009-52**; A61K028-18; A61K038-00; A61K038-22

ICS **A61K009-14**; **A61K009-50**; A61K038-19; A61K038-43; **A61K039-00**; **A61K039-395**; **A61K047-02**; **A61K047-30**

AB WO 9607399 A UPAB: 20020730

A sustained release compsn. comprises (a) a water-insoluble or slightly water-soluble polyvalent metal salt of a water-soluble peptide type of physiologically active substance except for an endothelin antagonist and (b) a biodegradable polymer.

USE - The peptide is e.g. a hormone, cytokine, haematopoietic factor, growth factor, enzyme, soluble or solubilized receptor, antibody, antigen-contg. peptide, blood coagulation factor or adhesion molecule, esp. a growth hormone, an insulin, a cytokine e.g. an interferon, or a growth factor, and the salt is pref. one with a transition metal or zinc.

ADVANTAGE - The compsn. efficiently incorporates water-soluble physiologically active substances, suppresses initial active substance burst, offers a constant active substance release rate and maintains substance activity.

Dwg.0/0

FS CPI

FA AB; DCN

MC CPI: A09-A07; A12-V01; B04-C01; B04-C03C; B04-H01; B04-H05; B04-H06; B04-H19; **B04-H20**; B04-J01; B04-J03A; B04-J05; B04-L01; B05-A03A; B05-A03B; B12-M10A

L83 ANSWER 27 OF 41 WPIX (C) 2002 THOMSON DERWENT

AN 1996-160135 [16] WPIX

DNC C1996-050520

TI Modulating cellular activity of tissue and cells expressing cell surface receptor for hyaluronic acid - using hyaluronic acid and its derivs. with other drugs for treating/preventing e.g. cancer, fibrosis etc..

DC A96 B04

IN ASCULAI, S S

PA (HYAL-N) HYAL PHARM CORP

CYC 66

PI WO 9606622 A1 19960307 (199616)* EN 47p A61K031-715

RW: AT BE CH DE DK ES FR GB GR IE IT KE LU MC MW NL OA PT SD SE SZ UG

W: AM AT AU BB BG BR BY CA CH CN CZ DE DK EE ES FI GB GE HU IS JP KE KG KP KR KZ LK LR LT LU LV MD MG MN MW MX NO NZ PL PT RO RU SD SE SG SI SK TJ TM TT UA UG US UZ VN

CA 2131130 A 19960301 (199624) A61K047-36 <--

AU 9531595 A 19960322 (199626) A61K031-715

ZA 9507223 A 19960626 (199631) 46p A61K000-00

CA 2145605 A 19960928 (199704) A61K031-725

EP 778776 A1 19970618 (199729) EN A61K031-715

R: AT BE CH DE DK ES FR GB GR IE IT LI LU MC NL PT SE

CN 1130532 A 19960911 (199801) A61K047-36 <--

HU 76846 T 19971229 (199819) A61K031-715

JP 10504828 W 19980512 (199829) 58p A61K031-725

KR 97705401 A 19971009 (199841) A61K031-715
ADT WO 9606622 A1 WO 1995-CA477 19950811; CA 2131130 A CA 1994-2131130 19940830; AU 9531595 A AU 1995-31595 19950811; ZA 9507223 A ZA 1995-7223 19950829; CA 2145605 A CA 1995-2145605 19950327; EP 778776 A1 EP 1995-927605 19950811, WO 1995-CA477 19950811; CN 1130532 A CN 1995-116995 19950829; HU 76846 T WO 1995-CA477 19950811, HU 1997-1507 19950811; JP 10504828 W WO 1995-CA477 19950811, JP 1996-508371 19950811; KR 97705401 A WO 1995-CA477 19950811, KR 1997-701164 19970224
FDT AU 9531595 A Based on WO 9606622; EP 778776 A1 Based on WO 9606622; HU 76846 T Based on WO 9606622; JP 10504828 W Based on WO 9606622; KR 97705401 A Based on WO 9606622
PRAI CA 1995-2145605 19950327; CA 1994-2131130 19940830
REP 09Jnl.Ref; EP 138572; US 4141973; WO 9104058; WO 9316732; WO 9321312
IC ICM A61K000-00; A61K031-715; A61K031-725; **A61K047-36**
ICS A61K007-06; A61K031-135; A61K031-14; A61K031-19; A61K031-375; A61K038-00; A61K038-21; **A61K039-395**; A61K045-00
AB WO 9606622 A UPAB: 19960422
A method for the modulation of cellular activity of tissue and cells expressing cell-surface receptor for a form of hyaluronic acid (HA) such as an adhesion mol. (e.g. **ICAM-1**, HARLEC and CD44) and/or a regulatory mol. (e.g. RHAMM) of a human, comprises administering: (a) a form of HA (e.g. HA, sodium hyaluronate or mol. wt. fractions of HA, homologues, analogues, derivs. complexes, esters, fragments or subunits of HA) or (b) a mol. which mimics these forms of HA in respect of their ability to bind to the same receptors as the form of HA, to a human to modulate cellular activity of tissues and/or cells expressing such high affinity cell-surface receptors, in an excipient.

Also claimed are: (1) the use of a form of HA to modulate cellular activity of tissues and/or cells expressing a high affinity cell-surface receptor for a form of HA in the human body and (2) the use of HA for treating/preventing disease.

USE - The method can be used for the treatment of e.g. colds, strokes, inflammation, fibrosis, cancer and metastases (all claimed). The HA forms can be used in doses of e.g. 10-1000 (esp. 50-500) mg/70 kg person, by e.g. parenteral or topical routes.

Dwg.0/8
FS CPI
FA AB; DCN
MC CPI: A03-A00A; A12-V01; B10-A07; B14-C03; **B14-H01B**; B14-N16

L83 ANSWER 28 OF 41 WPIX (C) 2002 THOMSON DERWENT
AN 1996-116786 [12] WPIX
DNC C1996-036962
TI Drug delivery compsn. for nasal admin. of antiviral agents - comprises inter-**cellular adhesion molecule** and bio-adhesive, useful for treatment of e.g. influenza and rhinoviral infections.
DC B04 B07
IN ILLUM, L; WATTS, P
PA (DANB-N) DANBIOSYST UK LTD; (ILLU-I) ILLUM L; (WATT-I) WATTS P
CYC 65
PI WO 9603142 A1 19960208 (199612)* EN 24p A61K038-17
RW: AT BE CH DE DK ES FR GB GR IE IT KE LU MC MW NL OA PT SD SE SZ UG
W: AM AT AU BB BG BR BY CA CH CN CZ DE DK EE ES FI GB GE HU IS JP KE KG KP KR KZ LK LR LT LU LV MD MG MN MW MX NO NZ PL PT RO RU SD SE SG SI SK TJ TM TT UA UG US UZ VN
AU 9529886 A 19960222 (199621) A61K038-17
NO 9700252 A 19970121 (199716) A61K000-00
FI 9700331 A 19970127 (199717) A61K000-00
GB 2305606 A 19970416 (199719) 1p A61K038-17
EP 773791 A1 19970521 (199725) EN A61K038-17
R: AT BE CH DE DK ES FR GB GR IE IT LI LU MC NL PT SE
GB 2305606 B 19980805 (199833) A61K038-17

ICS **A61K009-127**; A61K035-14; C12N005-08; G01N033-53
AB WO 9532734 A UPAB: 19960122
(A) A novel composition comprises at least one FcgammaRII (CD32) bridging agent which is characterised as impairing the capacity of antigen (Ag) presenting cells (APC's) to stimulate the activation of Ag-specific T-cells, resulting in Ag-specific T-cell un-responsiveness, and which is selected from: (a) aggregated human IgG mols.; (b) aggregated Fc fragments of human IgG mols.; (c) a bivalent monoclonal antibody (MAb) to the FcgammaRII; (d) a multivalent MAb to the FcgammaRII; (e) a functionally active fragment of the bivalent or multivalent MAb to the FcgammaRII; (f) a recombinant fusion protein of two or more human IgG Fc parts, or (g) a liposome vesicle comprising any of the above bridging agents. Also claimed are: (B) FcgammaRII-bridged professional APC`s obtainable by bridging professional APC`s with any of the FcgammaRII bridging agents above, and (C) a method for screening new FcgammaRII bridging agents comprising: (1) incubating cells from (B) in the absence or presence of possible FcgammaRII bridging agent, and (2) measuring the amt. of B7 1/2 and or **ICAM**-3 expression.
USE - The compsn. may be used in a medicament for the treatment and prevention of T-cell mediated diseases, and for the modulation of antigen-specific T-cell responsiveness. The compsn. is especially useful for the treatment of allergic disease, rejection of organs and tissues after transplantation, e.g. for inducing T-cell anergy or T-cell tolerance, and for the treatment of autoimmune disease. Target cells for treatment with the FcgammaRII bridging compsns. include human leukocytes, pref. macrophages, monocytes, dendritic cells, Langerhans cells or B cells. The compsn. is administered so that aggregated IgG antibodies are given at a dose between 1 mug/kg-20 mg/kg, pref. 1-7 mg/kg.
Dwg.0/8
FS CPI EPI
FA AB; DCN
MC CPI: B04-G21; B04-N0200E; B12-M11F; B14-G02A; B14-G02C; B14-G02D; D05-H09; D05-H11A
EPI: S03-E14H4

L83 ANSWER 30 OF 41 WPIX (C) 2002 THOMSON DERWENT
AN 1995-359859 [47] WPIX
DNN N1995-267490 DNC C1995-157360
TI Prodn. of autologous monoclonal antibody to self-antigen - using animals with an altered genome which does not produce at least one epitope of the self-antigen.
DC B04 D16 P14 S03
IN MUELLER, W; RAJEWSKY, K; ROES, J
PA (MILT-I) MILTENYI S
CYC 19
PI EP 677533 A2 19951018 (199547)* EN 16p C07K016-18
R: AT BE CH DE DK ES FR GB GR IE IT LI LU MC NL PT SE
CA 2146693 A 19951013 (199607) C12N015-13
JP 08056692 A 19960305 (199619) 13p C12P021-08
ADT EP 677533 A2 EP 1995-302440 19950412; CA 2146693 A CA 1995-2146693 19950410; JP 08056692 A JP 1995-87269 19950412
PRAI US 1994-226168 19940412
IC ICM C07K016-18; C12N015-13; C12P021-08
ICS A01K067-027; **A61K039-395**; **A61K047-48**; A61K051-10; C07K016-00; C07K016-42; C07K019-00; C12N005-00; C12N015-02; C12N015-20; G01N033-48; G01N033-50; G01N033-53; G01N033-531; G01N033-577
ICA C12N005-10
ICI C12P021-08, C12R001:91; C12N015-02, C12R001:
AB EP 677533 A UPAB: 19951128
Method (A) of obtaining an autologous monoclonal antibody (MAb) to a self-antigen (SA) from a non-human vertebrate animal comprises:(a) either: (i) altering the genome of the animal so that it does not produce 1

epitope of the SA, or
(ii) providing an animal whose genome has been altered so that it does not produce 1 epitope of the SA;(b) immunising the animal with the SA or a homologue;(c) collecting from the animal cells produced in response to and expressing antibodies against the SA or its homologue, and(d) producing antibodies using the collected cells or genetic material derived from the cells.

USE - The method can be used for obtaining MAbs to SAs such as cell surface antigens, cytokines, **cell adhesion mols**. or immunoglobulins (claimed). The MAbs can be used in immunoassays and as pharmaceutical agents, e.g. as receptor agonists or antagonists.

Dwg.0/4

FS CPI EPI GMPI
FA AB
MC CPI: B04-F05; B04-G21; B04-P01A0E; B14-L01; B14-L06; D05-H11A1; D05-H15
EPI: S03-E14H4

L83 ANSWER 31 OF 41 WPIX (C) 2002 THOMSON DERWENT
AN 1995-351323 [45] WPIX
DNC C1995-153903
TI New antibody of neutral isotype reactive with **E-selectin** - used in diagnosis and therapy of disorders involving increased **E-selectin** expression, esp. inflammatory disorders..
DC B04 D16
IN OWENS, R J; ROBINSON, M K; OWENS, J R
PA (CLLT) CELLTECH THERAPEUTICS LTD
CYC 65
PI WO 9526403 A1 19951005 (199545)* EN 63p C12N015-13
RW: AT BE CH DE DK ES FR GB GR IE IT KE LU MC MW NL OA PT SD SE SZ UG
W: AM AT AU BB BG BR BY CA CH CN CZ DE DK EE ES FI GB GE HU IS JP KE KG KP KR KZ LK LR LT LU LV MD MG MN MW MX NL NO NZ PL PT RO RU SD SE SG SI SK TJ TM TT UA UG US UZ VN
AU 9520769 A 19951017 (199604) C12N015-13
GB 2301366 A 19961204 (199701) 1p C07K016-28
EP 753065 A1 19970115 (199708) EN C12N015-13
R: AT BE CH DE DK ES FR GB GR IE IT LI LU MC NL PT SE
JP 09512705 W 19971222 (199810) 60p C12N015-09
NZ 282849 A 19980527 (199827) C12N015-13
GB 2301366 B 19980729 (199832) C07K016-28
AU 707440 B 19990708 (199938) C12N015-13
US 6204007 B1 20010320 (200118) C12N005-10
US 6407214 B1 20020618 (200244) C07K016-28
ADT WO 9526403 A1 WO 1995-GB692 19950328; AU 9520769 A AU 1995-20769 19950328; GB 2301366 A WO 1995-GB692 19950328, GB 1996-19691 19960920; EP 753065 A1 EP 1995-913225 19950328, WO 1995-GB692 19950328; JP 09512705 W JP 1995-525047 19950328, WO 1995-GB692 19950328; NZ 282849 A NZ 1995-282849 19950328, WO 1995-GB692 19950328; GB 2301366 B WO 1995-GB692 19950328, GB 1996-19691 19960920; AU 707440 B AU 1995-20769 19950328; US 6204007 B1 WO 1995-GB692 19950328, US 1996-718323 19961125; US 6407214 B1 Cont of WO 1995-GB692 19950328, Cont of US 1996-718323 19961125, US 2000-587526 20000605
FDT AU 9520769 A Based on WO 9526403; GB 2301366 A Based on WO 9526403; EP 753065 A1 Based on WO 9526403; JP 09512705 W Based on WO 9526403; NZ 282849 A Based on WO 9526403; GB 2301366 B Based on WO 9526403; AU 707440 B Previous Publ. AU 9520769, Based on WO 9526403; US 6204007 B1 Based on WO 9526403; US 6407214 B1 Cont of US 6204007
PRAI GB 1994-15331 19940729; GB 1994-6243 19940329
REP 02Jnl.Ref; EP 323806; EP 438312; WO 8807089; WO 9109967; WO 9322436
IC ICM C07K016-28; C12N005-10; C12N015-09; C12N015-13
ICS **A61K009-127**; **A61K039-395**; A61K049-00; C07K016-00
ICA C07K016-18; C12P021-08
AB WO 9526403 A UPAB: 19951114

An antibody (Ab) having specificity for **E-selectin**, characterised in that the Ab is a whole Ab of neutral isotype, is claimed.

USE - The Ab can be used for the treatment of a subject suffering from, or at risk of a disorder associated with increased **E-selectin** expression, partic. inflammatory disorders, e.g. psoriasis, dermatitis, inflammatory bowel disease, lung inflammatory disorders, arthritis, vasculitis, liver disease or thermal trauma. The Ab can also be used for inflamed site-specific delivery of agents. It can also be used in diagnostic applications.

ADVANTAGE - Since the whole Ab has a neutral isotype, the interaction with Fc receptors will be minimal so that Ab dependent cellular cytotoxicity, complement mediated lysis and immune responses in a host will be minimal. In partic, endothelial cell depletion is minimised using the Ab.

Dwg.0/19

FS CPI
FA AB
MC CPI: **B04-G01**; B04-G0100E; B12-K04A; B14-C04; B14-C09; B14-E10C; **B14-F02**; B14-K01; B14-N12; B14-N17C; D05-H09; D05-H11

L83 ANSWER 32 OF 41 WPIX (C) 2002 THOMSON DERWENT
AN 1995-006708 [01] WPIX
DNN N1995-005455 DNC C1995-002361
TI New compsn. comprising a complement moiety and a carbohydrate moiety - used for diagnosis and treatment of conditions involving inappropriate complement activity.
DC B04 D16 S03
IN RITTERSHAUS, C W; TOTH, C A
PA (TCEL-N) T CELL SCI INC; (AVAN-N) AVANT IMMUNOTHERAPEUTICS INC
CYC 45

PI	WO 9426786	A1	19941124 (199501)*		138p	C07K015-14
	RW: AT BE CH DE DK ES FR GB GR IE IT LU MC NL OA PT SE					
	W: AU BB BG BR BY CA CN CZ FI HU JP KR KZ LK MG MN MW NO NZ PL RO RU SD SK UA US					
	AU 9469475	A	19941212 (199522)			C07K015-14
	EP 730608	A1	19960911 (199641)	EN		C07K015-14
	R: AT BE CH DE DK ES FR GB GR IE IT LI LU MC NL PT SE					
	JP 08510257	W	19961029 (199705)		126p	C07K014-705
	AU 678486	B	19970529 (199730)			C07K015-14
	SG 52383	A1	19980928 (199903)			C07K015-14
	US 5856300	A	19990105 (199909)			A61K038-00
	US 5976540	A	19991102 (199953)		41p	A61K039-00 <--
	CA 2162600	C	20000711 (200044)	EN		C12P021-00
	US 6193979	B1	20010227 (200114)			A61K039-385 <--
	EP 730608	B1	20020327 (200222)	EN		C07K014-705
	R: AT BE CH DE DK ES FR GB GR IE IT LI LU MC NL PT SE					
	DE 69430253	E	20020502 (200237)			C07K014-705

ADT WO 9426786 A1 WO 1994-US5285 19940512; AU 9469475 A AU 1994-69475 19940512; EP 730608 A1 EP 1994-917961 19940512, WO 1994-US5285 19940512; JP 08510257 W JP 1994-525695 19940512, WO 1994-US5285 19940512; AU 678486 B AU 1994-69475 19940512; SG 52383 A1 SG 1996-3777 19940512; US 5856300 A WO 1994-US5285 19940512, US 1995-553339 19951111; US 5976540 A CIP of US 1993-61982 19930517, Cont of WO 1994-US5285 19940512, Cont of US 1995-553339 19951111, US 1998-61542 19980416; CA 2162600 C CA 1994-2162600 19940512, WO 1994-US5285 19940512; US 6193979 B1 CIP of US 1993-61982 19930517, Cont of WO 1994-US5285 19940512, US 1995-450274 19950525; EP 730608 B1 EP 1994-917961 19940512, WO 1994-US5285 19940512; DE 69430253 E DE 1994-630253 19940512, EP 1994-917961 19940512, WO 1994-US5285 19940512
FDT AU 9469475 A Based on WO 9426786; EP 730608 A1 Based on WO 9426786; JP 08510257 W Based on WO 9426786; AU 678486 B Previous Publ. AU 9469475, Based on WO 9426786; US 5856300 A Based on WO 9426786; CA 2162600 C Based on WO 9426786; EP 730608 B1 Based on WO 9426786; DE 69430253 E Based on EP 730608, Based on WO 9426786

PRAI US 1993-61982 19930517; US 1995-553339 19951111; US 1998-61542 19980416; US 1995-450274 19950525
REP 03Jnl.Ref
IC ICM A61K038-00; **A61K039-00**; **A61K039-385**; C07K014-705; C07K015-14; C12P021-00
ICS A61K037-00; A61K038-17; **A61K047-48**; C07K001-113; C07K002-00; C07K017-02; C07K017-10; G01N033-543; G01N033-564; G01N033-566
AB WO 9426786 A UPAB: 19950110
A compsn. is claimed comprising at least one complement moiety and at least one carbohydrate moiety. Also claimed is a soluble complement inhibitory protein (CIP) comprising a selectin ligand.
USE - The compsn. can be used in homing the complement moiety to adhesion molecules such as **selectins** on activated endothelium. They can be used for treating a subject with a disease or disorder involving undesirable or inappropriate complement activity (claimed). They can be used for treating **e**.g. inflammatory disorders, infectious disease, sepsis, autoimmune disease,etc. They can be used to study inflammatory and complement mediated diseases by virtue or their direct interaction with mediators of inflammation. In partic., the compsns. can be used for the diagnosis of inflammatory conditions (claimed).
ADVANTAGE - The compsns. localise the complement moiety to inflamed endothelium, allowing low dosage treatment. The compsns. can interrupt an initial event in the inflammatory response and have high persistence at the site of inflammation. The in vivo half life and/or bioavailability of the complement moiety is also prolonged.
Dwg.0/4
FS CPI EPI
FA AB; GI
MC CPI: B04-C02X; B04-H01; **B04-H20**; B04-N02; B14-A01; B14-A02; B14-C03; B14-C09B; B14-E10C; B14-F05; B14-F07; B14-G02; B14-G02C; B14-G02D; **B14-H01B**; B14-J01; B14-K01; B14-K01A; B14-N17C; B14-S07; D05-H09
EPI: S03-E14H4

L83 ANSWER 33 OF 41 WPIX (C) 2002 THOMSON DERWENT
AN 1995-000931 [01] WPIX
DNC C1995-000387
TI New monoclonal antibodies specific for CD2 - for inhibiting HIV-1 propagation in infected T cells without affecting immune response to other pathogens.
DC B04 D16
IN DIEGEL, M L; GILLILAND, L K; LEDBETTER, J A; LINSLEY, P S; MORAN, P A; ZARLING, J M
PA (BRIM) BRISTOL-MYERS SQUIBB CO
CYC 20
PI EP 626447 A1 19941130 (199501)* EN 35p C12N015-13
R: AT BE CH DE DK ES FR GB GR IE IT LI LU MC NL PT SE
CA 2124126 A 19941126 (199509) C12P021-08
JP 07147983 A 19950613 (199532) 23p C12N015-09
US 5795572 A 19980818 (199840) C07K016-28
US 5807734 A 19980915 (199844) C07H021-04
US 6384198 B1 20020507 (200235) C07K016-28
ADT EP 626447 A1 EP 1994-108104 19940525; CA 2124126 A CA 1994-2124126 19940524; JP 07147983 A JP 1994-111160 19940525; US 5795572 A US 1993-68946 19930525; US 5807734 A Div ex US 1993-68946 19930525, US 1995-456221 19950531; US 6384198 B1 Div ex US 1993-68946 19930525, US 1995-443888 19950531
FDT US 6384198 B1 Div ex US 5795572
PRAI US 1993-68946 19930525; US 1995-456221 19950531; US 1995-443888 19950531
REP 04Jnl.Ref; WO 9111194; WO 9306866
IC ICM C07H021-04; C07K016-28; C12N015-09; C12N015-13; C12P021-08

ICS A01N001-02; A61K035-18; **A61K039-395**; **A61K039-44**; **A61K047-48**; A61M001-36; C07K015-28; C07K016-46; C12N001-20; C12N001-21; C12N015-11; G01N033-53
ICI C12N015-09, C12R001:19
AB EP 626447 A UPAB: 19950110
New monoclonal antibodies (MAb) with specific affinity for CD2 is (a) chimaeric MAb CD2 SFv-Ig obtained by expressing a construct cloned in recombinant E.coli ATCC 69277; (b) MAb with complementarity determining regions (CDR) identical to those of a CD2-specific antibody or (c) MAb that compete with CD2 SFv-Ig for binding to CD2 at least 80% (esp. 90%) as effectively on a molar basis as CD2 SFv-Ig. Also new are (1) modified forms of MAb in which at least part of the Ig-derived amino acid sequence is altered or deleted, or the entire Ig-derived region is deleted; (2) recombinant E. coli ATCC 69277 transformed by a construct able to express CD2 SFv-Ig chimaeric, humanised MAb in mammalian cells and (3) cDNA construct expressing such MAb, having murine CDR and human constant regions.

USE - MAb disrupt cell surface interactions with CD4 positive lymphocytes and monocytes so are able to inhibit prodn. of HIV-1 virus in infected T cells. More generally other antibodies to CD2, CD18 or the counter receptors LFA-3 or **ICAM-1**, or a ligand contg. the extracellular domain of LFA-3 in soluble form, can be used similarly. Alternatively T cells from a subject infected with HIV-1 are treated with MAb, then used to treat patients to reduce complications (opportunistic infections) associated with HIV-1, i.e. to increase the proportion of functional, non-HIV-1 producing T cells. Treatment with MAb may be combined with admin. of an agent (A) for control of opportunistic infections. MAb can also be used for diagnosis.

ADVANTAGE - Treatment with MAb has no significant effect on immune function or response to pathogens other than HIV-1 and MAb are not appreciably immunogenic.

Dwg.3/3
FS CPI
FA AB; GI
MC CPI: B04-F10A3E; B04-G08; B04-G21; B14-A02B1; D05-H11A2; D05-H12; D05-H12B2; D05-H14A1

L83 ANSWER 34 OF 41 WPIX (C) 2002 THOMSON DERWENT
AN 1994-026146 [03] WPIX
DNC C1994-012082
TI Multimeric forms of inter-**cellular adhesion mol**. (**ICAM**) - displaying enhanced binding of human rhinovirus and able to reduce its infectivity.
DC B04 D16
IN GREVE, J M; MCCLELLAND, A
PA (MILE) MILES INC; (FARB) BAYER CORP
CYC 27
PI WO 9400485 A1 19940106 (199403)* EN 70p C07K007-00
RW: AT BE CH DE DK ES FR GB GR IE IT LU MC NL PT SE
W: AU CA FI HU JP KR NO PL RU
AU 9345432 A 19940124 (199420) C07K007-00
EP 604624 A1 19940706 (199426) EN C07K007-00
R: AT BE CH DE DK ES FR GB GR IE IT LI LU MC NL PT SE
JP 06510208 W 19941117 (199505) C12P021-02
NO 9404966 A 19941221 (199511) C07K014-705
FI 9406006 A 19941221 (199512) A61K000-00
AU 9671746 A 19970130 (199713) C12N007-04
AU 675441 B 19970206 (199714) C07K015-06
EP 604624 A4 19970312 (199729) C07K007-00
HU 75827 T 19970528 (199805) C07K007-00
AU 710965 B 19990930 (199952) C12N007-04
US 6130202 A 20001010 (200052) A61K038-04
ADT WO 9400485 A1 WO 1993-US5972 19930622; AU 9345432 A AU 1993-45432

19930622; EP 604624 A1 EP 1993-915452 19930622, WO 1993-US5972 19930622; JP 06510208 W WO 1993-US5972 19930622, JP 1994-502541 19930622; NO 9404966 A WO 1993-US5972 19930622, NO 1994-4966 19941221; FI 9406006 A WO 1993-US5972 19930622, FI 1994-6006 19941221; AU 9671746 A Div ex AU 1993-45432 19930622, AU 1996-71746 19961113; AU 675441 B Add to AU 1991-81176 19910717, AU 1993-45432 19930622; EP 604624 A4 EP 1993-915452 ; HU 75827 T WO 1993-US5972 19930622, HU 1994-3720 19930622; AU 710965 B Div ex AU 1993-45432 19930622, AU 1996-71746 19961113; US 6130202 A CIP of US 1990-556238 19900720, CIP of US 1991-704984 19910524, Cont of US 1992-903069 19920622, US 1994-227496 19940414

FDT AU 9345432 A Based on WO 9400485; EP 604624 A1 Based on WO 9400485; JP 06510208 W Based on WO 9400485; AU 675441 B Previous Publ. AU 9345432, Based on WO 9400485; HU 75827 T Based on WO 9400485; AU 710965 B Div ex AU 675441, Previous Publ. AU 9671746

PRAI US 1992-903069 19920622; US 1990-556238 19900720; US 1991-704984 19910524; US 1994-227496 19940414

REP 3.Jnl.Ref; 2.Jnl.Ref; EP 365837; EP 387701; EP 468257

IC ICM A61K000-00; A61K038-04; C07K007-00; C07K014-705; C07K015-06; C12N007-04; C12P021-02

ICS A61K037-02; A61K038-08; A61K038-10; A61K038-16; A61K038-17; **A61K039-00**; **A61K047-30**; **A61K047-42**; C07K005-08; C07K009-00; C07K013-00; C07K014-47; C07K017-00; C07K017-10; C12N007-06

AB WO 9400485 A UPAB: 19950721

Multimeric **intercellular adhesion molecule** (**ICAM**) (I) is new. **ICAM** is pref. non-transmembrane **ICAM** (tICAM), pref. without the carboxyl intracellular domain and without the hydrophobic membrane domain. In a method for enhancing the binding of **ICAM** to a ligand the improvement comprises presenting the **ICAM** in a multimeric configuration.

Also claimed is a method for inducing irreversible uncoating of human rhinovirus by contacting the human rhinovirus with **ICAM-1** or a tICAM fragment, this method also being claimed for irreversibly inhibiting infectivity of a mammalian cell by a human rhinovirus.

USE/ADVANTAGE - (I) display enhanced binding of human rhinovirus (HRV) and are able to reduce HRV infectivity, as well as the infectivity of other viruses known to bind to the ''major'' gp. human rhinovirus receptor (HRR). (I) may also be used ot block tICAM interaction with lymphocyte function-associated antigen-1 (LFA-1).

Dwg.0/7

Dwg.0/7

FS CPI

FA AB; DCN

MC CPI: B04-C02A3; B04-C03B; **B04-G01**; B04-H02D; B04-N02; B04-N06; B14-A02B3; B14-L06; D05-H10; D05-H17B6

L83 ANSWER 35 OF 41 WPIX (C) 2002 THOMSON DERWENT

AN 1993-017908 [02] WPIX

DNN N1993-013688 DNC C1993-008160

TI Inter-**cellular adhesion molecule**-3 inhibiting granulocyte, lymphocyte and macrophage adhesion - for treating inflammation, AIDS, asthma, auto-immune thyroiditis, multiple sclerosis, ARDS etc..

DC B04 D16 S03

IN DEFOUGEROLLES, A R; SPRINGER, T A; TIMOTHY, A; DE, FOUGEROLLES A R

PA (BLOO-N) CENT BLOOD RES INC; (BLOO-N) CENT BLOOD RES

CYC 35

PI WO 9222323 A1 19921223 (199302)* EN 123p A61K039-00 <--
RW: AT BE CH DE DK ES FR GB GR IT LU MC NL SE
W: AU BG BR CA CS FI HU JP KR NO PL RO RU US

AU 9222376 A 19930112 (199317) A61K039-00 <--

ZA 9204276 A 19930331 (199319) 10p A61K000-00

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     CN 1069522    A  19930303 (199402)              C12P021-00
     EP 590051     A1 19940406 (199414)  EN          A61K039-00      <--
        R: AT BE CH DE DK ES FR GB GR IT LI LU MC NL SE
     FI 9305500    A  19940209 (199416)              A61K000-00
     NO 9304491    A  19940211 (199416)              A61K013-00
     CZ 9302702    A3 19940817 (199435)              C12N015-00
     SK 9301395    A3 19941005 (199444)
     JP 06509706   W  19941102 (199503)              C12N015-12
     HU 66617      T  19941228 (199506)              C12N015-12
     BR 9206142    A  19941227 (199508)              C12N015-11
     NZ 243114     A  19950328 (199519)              C07K013-00
     EP 590051     A4 19941012 (199534)
     AU 670243     B  19960711 (199635)              C12N015-12
     US 5629162    A  19970513 (199725)       56p    G01N033-53
     CZ 283478     B6 19980415 (199821)              C12N015-00
     US 5891841    A  19990406 (199921)#             A61K038-17
     SK 279937     B6 19990611 (199930)              C12N015-00
     HU 217176     B  19991228 (200010)              C12N015-12
     RO 115415     B  20000228 (200020)              A61K039-00      <--
     RU 2130782    C1 19990527 (200027)              A61K048-00
     IL 102176     A  20010913 (200158)              C12N015-12
     KR 291844     B  20010917 (200231)              A61K039-00      <--
     JP 3288042    B2 20020604 (200240)       52p    C12N015-09
ADT  WO 9222323 A1 WO 1992-US4896 19920611; AU 9222376 A AU 1992-22376
     19920611; ZA 9204276 A ZA 1992-4276 19920611; CN 1069522 A CN 1992-105126
     19920611; EP 590051 A1 EP 1992-914138 19920611, WO 1992-US4896 19920611;
     FI 9305500 A WO 1992-US4896 19920611, FI 1993-5500 19931208; NO 9304491 A
     WO 1992-US4896 19920611, NO 1993-4491 19931209; CZ 9302702 A3 CZ 1993-2702
     19920611; SK 9301395 A3 WO 1992-US4896 19920611, SK 1993-1395 19931210; JP
     06509706 W WO 1992-US4896 19920611, JP 1993-500999 19920611; HU 66617 T WO
     1992-US4896 19920611, HU 1993-3529 19920611; BR 9206142 A BR 1992-6142
     19920611, WO 1992-US4896 19920611; NZ 243114 A NZ 1992-243114 19920611; EP
     590051 A4 EP 1992-914138          ; AU 670243 B AU 1992-22376 19920611; US
     5629162 A CIP of US 1991-712879 19910611, Cont of WO 1992-US4896 19920611,
     Cont of US 1992-38990 19921223, US 1995-473981 19950607; CZ 283478 B6 WO
     1992-US4896 19920611, CZ 1993-2702 19920611; US 5891841 A CIP of US
     1991-712879 19910611, Div ex US 1992-38990 19921223, US 1995-474087
     19950607; SK 279937 B6 WO 1992-US4896 19920611, SK 1993-1395 19920611; HU
     217176 B WO 1992-US4896 19920611, HU 1993-3529 19920611; RO 115415 B WO
     1992-US4896 19920611, RO 1993-1672 19920611; RU 2130782 C1 WO 1992-US4896
     19920611, RU 1993-58655 19920611; IL 102176 A IL 1992-102176 19920611; KR
     291844 B WO 1992-US4896 19920611, KR 1993-703828 19931211; JP 3288042 B2
     WO 1992-US4896 19920611, JP 1993-500999 19920611
FDT  AU 9222376 A Based on WO 9222323; EP 590051 A1 Based on WO 9222323; JP
     06509706 W Based on WO 9222323; HU 66617 T Based on WO 9222323; BR 9206142
     A Based on WO 9222323; AU 670243 B Previous Publ. AU 9222376, Based on WO
     9222323; CZ 283478 B6 Previous Publ. CZ 9302702, Based on WO 9222323; SK
     279937 B6 Previous Publ. SK 9301395; HU 217176 B Previous Publ. HU 66617,
     Based on WO 9222323; RO 115415 B Based on WO 9222323; RU 2130782 C1 Based
     on WO 9222323; KR 291844 B Previous Publ. KR 94701876; JP 3288042 B2
     Previous Publ. JP 06509706, Based on WO 9222323
PRAI US 1991-712879   19910611; US 1992-38990    19921223; US 1995-473981
     19950607; US 1995-474087   19950607
REP  9.Jnl.Ref; 4.Jnl.Ref; EP 387668
IC   ICM  A61K000-00; A61K013-00; A61K038-17; A61K039-00; A61K048-00;
          C07K013-00; C12N015-00; C12N015-09; C12N015-11; C12N015-12;
          C12P021-00; G01N033-53
     ICS  A61K037-00; A61K037-02; A61K039-395; A61K047-48;
          A61K049-00; C07H021-00; C07K003-00; C07K003-10; C07K003-100;
          C07K003-12; C07K007-10; C07K014-705; C07K015-00; C07K015-06;
          C07K015-12; C07K015-14; C07K015-28; C07K016-18; C12N005-12;
          C12N005-16; C12N005-20; C12N005-22; C12N005-24; C12N015-06;
          C12N015-19; C12P021-08; C12Q001-00; C12Q001-68; G01N033-50;
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G01N033-567; G01N033-569; G01N033-571; G01N033-574; G01N033-577; G01N033-68

AB WO 9222323 A UPAB: 19931118

Intercellular adhesion molecule-3 (**ICAM**-3) or a functional deriv., free of natural contaminants is new.

Also claimed are; (1) recombinant DNA molecule encoding **ICAM** -3; (2) an antibody or fragment specific for **ICAM**-3 or a fragment; (3) a hybridoma producing this monoclonal Ab; (4) modulating **ICAM**-3 biological functions of a cell by admin. of an **ICAM** -3 modulating agent from the Ab or fragment of (2)m **ICAM**-3 or deriv. or a non-immunoglobulin antagonist of **ICAM**-3 other than **ICAM-1**, **ICAM**-2 or a member of the CD-18 family; (5) suppression of infection of leukocytes with HIV by admin. of an HIV-1 infection suppression agent from an Ab or fragment specific for **ICAM**-3, a toxin-derivatisation of the Ab or fragment, **ICAM** -3 or deriv., a non-immunoglobulin antagonist as above, or a toxin-derivatised mmember of the CD18 family or a deriv. of this; (6) suppression of growth of an **ICAM**-3 expressing tumour by admin. of an agent as in (5); (7) suppression of growth of a tumour expressing lymphocyte function-associated antigen-1 by admin. of a toxin-derivated **ICAM**-3 of fragment; (8) a pharmaceutical compsn. comprising an agent as listed in (4) or (5) opt. with an immunosuppressive agent.

USE/ADVANTAGE - The Ab or fragment can be used to diagnose **ICAM**-3 expressing tumour cells, inflammation and the presence of **ICAM**-3 in a fluid. The DNA may also be used to detect **ICAM** -3 expressing cells. The inflammation is in response to delayed type hypersensitivity, psoriasis, organ transplant, e.g. solid (pref. kidney) or non-solid (pre. bone marrow) transplants, autoimmune disease, pref. Raynaud's syndrome, autoimmune thyroidosis, EAE, multiple sclerosis, rheumatoid arthritis and lupus erythematosus, tissue graft rejection, a non-specific inflammation in response to adult respiratory distress syndrome, multiple organ injury syndromes secondary to septicaemia, trauma or haemorrhage, reperfusion injury of myocardium or other tissues, acute glomerulonephritis, reactive arthritis, dermatoses with acute inflammatory components, acute purulent meningitis or other CNS inflammatory disorders, e.g. stroke, thermal injury, haemodialysis leukopheresis, ulcerative colitus, Crohn's disease, necrotising enterocolitis, granulocyte tranfusion associated syndromes or cytokine-induced toxicity. The **ICAM**-3 mediated function is metastasis of a haematopoietic tumour cell requiring a CD-18 molecule for migration, the migration of a virally-infected leukocyte, or the migration of cells associated with an asthmatic response. The virus is HIV. The method may also be used to suppress T cell death and syncytia formation in HIV infection

Dwg.1A/18

FS CPI EPI

FA AB; GI; DCN

MC CPI: B04-B04A1; B04-B04A3; **B04-B04C5**; **B04-B04C6**; B04-B04J; B12-A06; **B12-G07**; B12-K04A; D05-C12; D05-H03B; D05-H09; D05-H11; D05-H12

EPI: S03-E14H4

ABEQ ZA 9204276 A UPAB: 19931113

The new **intercellular adhesion molecules** (**ICAM**-3) are involved in the process through which lymphocytes recognise and migrate to sites of inflammation as well as attach to cellular substrates during inflammation.

Further claimed are screening assays for identifying the molecules, antibodies capable of binding the molecules.

USE - For therapeutic and diagnostic use.

ABEQ US 5629162 A UPAB: 19970619

A method of identifying agents capable of antagonizing **ICAM**-3 binding to LFA-1, comprising the steps of:

contacting **ICAM**-3 with LFA-1 in the presence of a compound;

measuring **ICAM**-3/LFA-1 binding in the presence of said compound;

wherein decreased binding compared to binding in the absence of said compound identifies said compound as an antagonist of **ICAM**-3 binding to LFA-1.

Dwg.0/20

L83 ANSWER 36 OF 41 WPIX (C) 2002 THOMSON DERWENT
AN 1992-131888 [16] WPIX
CR 1992-268378 [32]; 1993-100995 [12]
DNC C1992-061710
TI Novel pharmaceutical delivery via the neural system - by admin. of active agent in nerve adhesion moiety, used for diagnosis and treatment of nerve injuries and compression.
DC B04 B06 K08
IN FILLER, A G; FILLER, A; LEVER, A M L; LEVER, A M
PA (SGEO-N) ST GEORGES ENTERPRISES LTD; (SYNG-N) SYNGENIX LTD; (SGEO-N) ST GEORGES ENTR LTD
CYC 22
PI WO 9204916 A 19920402 (199216)* FR 999p
RW: AT BE CH DE DK ES FR GB GR IT LU NL SE
W: AU CA JP NO US
AU 9185142 A 19920415 (199230) A61K047-48 <--
EP 548157 A1 19930630 (199326) EN 123p A61K047-48 <--
R: AT BE CH DE DK ES FR GB GR IT LI LU NL SE
EP 566590 A1 19931027 (199343) EN A61K009-51 <--
R: BE CH DE DK ES FR GB GR IT LI NL SE
FI 9400923 A 19940225 (199418) C12Q000-00
NO 9400658 A 19940225 (199419) C12N009-12
EP 601010 A1 19940615 (199423) EN C12Q001-48
R: BE CH DE DK ES FR GB GR IE IT LI MC NL SE
WO 9204916 A3 19920820 (199511)
US 5554498 A 19960910 (199642) 12p C12P019-34
US 5614652 A 19970325 (199718) 30p C07F015-00
EP 548157 B1 19980520 (199824) EN 13p A61K047-48 <--
R: AT BE CH DE DK ES FR GB GR IT LI LU NL SE
DE 69129463 E 19980625 (199831) A61K047-48 <--
EP 861667 A2 19980902 (199839) EN A61K047-48 <--
R: DE FR GB
US 5948384 A 19990907 (199943) A61K051-00
ADT WO 9204916 A WO 1991-EP1780 19910913; AU 9185142 A AU 1991-85142 19910913, WO 1991-EP1780 19910913; EP 548157 A1 EP 1991-916129 19910913, WO 1991-EP1780 19910913; EP 566590 A1 EP 1992-901269 19920104, WO 1992-EP21 19920104; FI 9400923 A WO 1992-GB1599 19920901, FI 1994-923 19940225; NO 9400658 A WO 1992-GB1599 19920901, NO 1994-658 19940225; EP 601010 A1 EP 1992-918221 19920901, WO 1992-GB1599 19920901; WO 9204916 A3 WO 1991-EP1780 19910913; US 5554498 A WO 1992-GB1599 19920901, US 1994-204144 19940228; US 5614652 A WO 1992-EP21 19920104, US 1993-87781 19931005; EP 548157 B1 EP 1991-916129 19910913, WO 1991-EP1780 19910913, Related to EP 1997-119199 19910913; DE 69129463 E DE 1991-629463 19910913, EP 1991-916129 19910913, WO 1991-EP1780 19910913; EP 861667 A2 Div ex EP 1991-916129 19910913, EP 1997-119199 19910913; US 5948384 A Div ex US 1993-988919 19930405, US 1995-473697 19950607
FDT AU 9185142 A Based on WO 9204916; EP 548157 A1 Based on WO 9204916; EP 566590 A1 Based on WO 9211846; EP 601010 A1 Based on WO 9305174; US 5554498 A Based on WO 9305174; US 5614652 A Based on WO 9211846; EP 548157 B1 Based on WO 9204916; DE 69129463 E Based on EP 548157, Based on WO 9204916; EP 861667 A2 Div ex EP 548157
PRAI GB 1991-18676 19910830; GB 1990-20075 19900914; GB 1990-23580 19901030; GB 1990-27293 19901217; GB 1991-233 19910107; GB 1991-981 19910116; GB 1991-2146 19910131; GB 1991-10876 19910520; GB 1991-16373 19910730; GB 1991-17851 19910819; GB 1991-19665 19910913; GB 1991-23677 19911107; GB 1992-5470

19920313; GB 1992-6402 19920324
REP 4.Jnl.Ref; No-SR.Pub; US 4827945; WO 8601112; WO 8800060; WO 8909625; WO 9001295; 1.Jnl.Ref; DE 3711724; JP 01200605; US 4001014; US 4101435; WO 9007322; EP 386857
IC ICM **A61K009-51**; **A61K047-48**; A61K051-00; C07F015-00; C12N009-12; C12P019-34; C12Q000-00; C12Q001-48
ICS A61K049-00; A61M036-14; C07F015-02; C12N009-99; C12Q001-00; C12Q001-68; C12Q001-70
AB WO 9204916 A UPAB: 19991020
(+30.10.90, 17.12.90, 07.01.91, 16.01.91, 31.01.91, 20.05.90, 30.07.91, 19.08.91-GB-023580, 027293, 000233, 000981, 002146, 010876, 016373, 017851)

New treatment of the living human or non-human body to effect (a) a desired therapeutic or prophylactic treatment; or (b) assist diagnostic or surgical treatment; comprises admin., into a vascularised peripherally innervated tissue site, or into other tissue sites innervated by a spinal root, a particulate pharmaceutical agent, comprising a nerve adhesion moiety (NAM), and a physiologically active or diagnostic marker moiety, capable of axonal transport from the tissue site.

USE/ADVANTAGE - Method can be used to check for sciatica to show the exact place of nerve root compression, without, as in myelography lumbar puncture, hospitalisation, or (using mRI) and X-ray exposure or discomfort. Other nerve compression and entrapment syndromes which can be investigated include carpal tunnel syndrome, trigeminal neuralgia, Glossopharyngeal neuralgia, hemi-facial spasm, vertigo/Meiurere's disease, hypertension due to vagal compression, cervical radiculopathy, incontinence and impotence problens, localisation of nerve bruises and lacerations, assessment of spinal cord injury, evaluation of neuropathies e.g. in diabetes, neuropathy due to tumours or metastases or tumours, Alzheimer's disease, imaging of epileptic foci and verification of denervation

Dwg.0/23

FS CPI
FA AB; DCN
MC CPI: B04-A04; B04-B02B4; B04-B02C; B04-B04A4; B04-B04A5; B04-B04A6; **B04-B04C**; B04-B04J; B04-C01; B04-C02C; B04-D02; B05-A03; B05-A04; B11-C08; B12-D07; **B12-E01**; B12-K04A; B12-K07; K09-B; K09-E
ABEQ EP 548157 A UPAB: 19931116
New treatment of the living human or non-human body to effect (a) a desired therapeutic or prophylactic treatment; or (b) assist diagnostic or surgical treatment; comprises admin., into a vascularised peripherally innervated tissue site, or into other tissue sites innervated by a spinal root, a particulate pharmaceutical agent, comprising a nerve adhesion moiety (NAM), and a physiologically active or diagnostic marker moiety, capable of axonal transport from the tissue site.

USE/ADVANTAGE - To check for sciatica to show the exact place or nerve root compression, without, as in myelography lumber puncture, hospitalisation, or (using mRI) and X-ray exposure or discomfort. Other nerve compression and entrapment syndromes which can be investigated include carpal tunnel syndrome, trigeminal neuralgia. Glossopharyngeal neuralgia hemi-facial spasm, vertigo/Meiurere's disease, hypertension due to vagal compression, cervical radiculopathy, incontinence and impotence problems, localisation of nerve bruises and lacerations, assessment of spinal cord injury, evaluation of neuropathies e.g. in diabetes, neuropathy due to tumours or metastases or tumours, Alzheimer's disease, imaging of epileptic foci and verification of denervation.

ABEQ EP 566590 A UPAB: 19931207
Use of new pharmaceutical compsns. contg. endocytosable particles of a physiologically tolerable material contg. atoms or ions of a therapeutically or prophylactically effective element is claimed. Use of compsns. comprising particles capable of being endocytosed and of subsequent intracellular release of metal cations which compete with

cations native to the endocytosing cells and which are detectable from outside the cells, and a crystalline material comprising Pd in an Fe oxide matrix are also claimed. Prodn. of modified spinel and garnet particles by precipitating di- and trivalent metal ions from a soln. contg. an element having a desired therapeutic or prophylactic activity, and opt. conjugating the resulting particles with a **cell adhesion mol.**, opt. after size sepn. and coating is also new.

USE - Suppression of viral (e.g. HIV) replication in cells such as macrophages.

ABEQ US 5554498 A UPAB: 19961021

A kit of two or more containers packaged together, the contents comprising an IUPAC Group 3 ion, or a salt thereof, wherein said Group 3 ion is selected from the group consisting of scandium ion and lanthanum ion, and at least one reagent selected from the group consisting of:

(a) a nucleic add polymerase,

(b) a template, and

(c) a buffer solution having a pH that is substantially the optimum for the polymerase activity of said nucleic acid polymerase.

Dwg.1/1

ABEQ US 5614652 A UPAB: 19970502

A particle comprising palladium disposed within an iron oxide matrix.

Dwg.0/14

L83 ANSWER 37 OF 41 WPIX (C) 2002 THOMSON DERWENT

AN 1992-064896 [08] WPIX

CR 1994-183500 [22]; 1997-154206 [14]

DNC C1992-029753

TI New peptide(s) derived from lectin-like domain of GMP-140 - inhibit GMP-140 binding of neutrophil(s) and monocytes and are useful in modulating inflammatory responses and diagnosing GMP-140 disorders.

DC B04 D16

IN MCEVER, R P

PA (OKLA) UNIV OKLAHOMA STATE; (OKLA) UNIV OF OKLAHAMA; (UYOK-N) UNIV OKLAHOMA; (OKLA) UNIV OKLAHOMA

CYC 18

PI

WO 9201718	A	19920206 (199208)*				
RW: AT BE CH DE DK ES FR GB GR IT LU NL SE						
W: AU CA JP						
AU 9186207	A	19920218 (199222)			C07K015-00	
US 5198424	A	19930330 (199315)		17p	A61K037-00	
EP 544815	A1	19930609 (199323)	EN	66p	C07K015-00	
R: AT BE CH DE DK ES FR GB GR IT LI LU NL SE						
JP 05509330	W	19931222 (199405)		22p	C07K007-08	
US 5378464	A	19950103 (199507)#			A61K039-395	<--
WO 9201718	A3	19920514 (199510)				
AU 660627	B	19950706 (199534)			C07K007-08	
AU 9517731	A	19950706 (199534)			C08B037-00	
EP 714912	A2	19960605 (199627)	EN	7p	C07K014-705	
R: AT BE CH DE DK ES FR GB GR IT LI LU NL SE						
EP 714912	A3	19960626 (199635)				
US 5767241	A	19980616 (199831)#			C07K014-00	
AU 697488	B	19981008 (199901)			C08B037-00	
JP 11147900	A	19990602 (199932)		26p	C07K016-18	
US 5919637	A	19990706 (199933)#			G01N033-53	
US 5929036	A	19990727 (199936)			C07K001-00	
JP 3096305	B2	20001010 (200052)		27p	C07K014-705	
JP 2001197899	A	20010724 (200147)		27p	C12P021-08	
CA 2086323	C	20020514 (200240)	EN		C07K014-705	

ADT AU 9186207 A AU 1991-86207 19910717, WO 1991-US5059 19910717; US 5198424 A CIP of US 1989-320408 19890308, Cont of US 1990-554199 19900717, US 1992-867271 19920407; EP 544815 A1 EP 1991-916882 19910717, WO 1991-US5059 19910717; JP 05509330 W JP 1991-517240 19910717, WO 1991-US5059 19910717; US 5378464 A US 1989-320408 19890308; WO 9201718 A3 WO 1991-US5059

19910717; AU 660627 B AU 1991-86207 19910717; AU 9517731 A Div ex AU 1991-86207 19910717, AU 1995-17731 19950428; EP 714912 A2 Div ex EP 1991-916882 19910717, EP 1995-202380 19910717; EP 714912 A3 Div ex EP 1991-916882 19910717, EP 1995-202380 19910717; US 5767241 A Cont of US 1989-320408 19890308, US 1994-272224 19940708; AU 697488 B Div ex AU 1991-86207 19910717, AU 1995-17731 19950428; JP 11147900 A Div ex JP 1991-517240 19910717, JP 1998-219500 19910717; US 5919637 A Cont of US 1989-320408 19890308, Div ex US 1994-272224 19940708, US 1995-449295 19950524; US 5929036 A CIP of US 1989-320408 19890308, CIP of US 1990-554199 19900717, Cont of US 1991-650484 19910205, Div ex US 1994-278554 19940721, US 1995-469543 19950606; JP 3096305 B2 JP 1991-517240 19910717, WO 1991-US5059 19910717; JP 2001197899 A Div ex JP 1998-219500 19910717, JP 2000-356784 19910717; CA 2086323 C CA 1991-2086323 19910717, WO 1991-US5059 19910717

FDT AU 9186207 A Based on WO 9201718; EP 544815 A1 Based on WO 9201718; JP 05509330 W Based on WO 9201718; AU 660627 B Previous Publ. AU 9186207, Based on WO 9201718; US 5767241 A Cont of US 5378464; AU 697488 B Previous Publ. AU 9517731; US 5919637 A Cont of US 5378464, Div ex US 5767241; US 5929036 A CIP of US 5378464; JP 3096305 B2 Previous Publ. JP 05509330, Based on WO 9201718; CA 2086323 C Based on WO 9201718

PRAI US 1991-650484 19910205; US 1990-554199 19900717; US 1989-320408 19890308; US 1992-867271 19920407; US 1994-272224 19940708; US 1995-449295 19950524; US 1994-278554 19940721; US 1995-469543 19950606

REP No-SR.Pub; 11Jnl.Ref; US 4783330; WO 9106632; NoSR.Pub

IC ICM A61K037-00; **A61K039-395**; C07K001-00; C07K007-08; C07K014-00; C07K014-705; C07K015-00; C07K016-18; C08B037-00; G01N033-53

ICS A61K031-02; A61K031-70; A61K037-02; A61K038-00; A61K038-10; A61K038-17; A61K038-36; **A61K039-39**; A61K043-00; **A61K047-48**; A61K049-00; A61K049-02; A61L027-00; A61P029-00; A61P035-04; C07H013-04; C07K002-00; C07K005-00; C07K007-00; C07K007-06; C07K015-06; C07K015-12; C07K016-28; C07K016-46; C07K017-00; C07K017-02; C12N015-09; G01N033-537

ICA C12N015-02; C12P021-08

AB WO 9201718 A UPAB: 20020626

An isolated peptide derived from the lectin-like domain of granule membrane protein 140 (GMP-14) inhibiting bindering of neutrophils and monocytes to GMP-140; the peptide may be CQNRYTOLVAJQNKNE (I) AENWADNEPNNKRNNED, RKNNKTWTWVGTKKALTNE, KKALTNEAENWAD and portions of these inhibiting binding of neutrophils and monocytes to GMP-140.

Also claimed are: an isolated carbohydrate binding to a **selectin**, where the carbohydrate comprises an alpha 1,3-fucosylated, alpha 2,3-sialyated lactosaminoglycan structure; the carbohydrate may be (i) silyl Lex, difucosyl silyl Lex or longer polyfucosylated polyactosaminoglycans or (ii) NeuAcalpha 2, 3 Galbeta1, 4 (Fuc alpha 1,3)GlcNAc beta1-R, where R is a protein or other carbohydrate structure; (C) a method for modulating an inflammatory response; (D) an antibody to an isolated carbohydrate binding to a **selectin**; (**E**) an isolated protein component of a ligand for **selectins**

.

USE/ADVANTAGE - The peptides, carbohydrate structures and antibodies can be used for the detection of human disorders in which GMP-140 or GMP-140 ligands may be defective. They can also be used in the modulation or inhibition of coagulation processes or inflammatory processes, e.g. in the treatment of injury from ischaemia and reperfusion, bacterial sepsis and disseminated intravascular coagulation, adult respiratory distress syndrome, tumour metastasis, rheumatoid arthritis and atherosclerosis.

0/7

FS CPI

FA AB; DCN

MC CPI: B04-B04A; **B04-B04C6**; B04-C01; B04-C02; B12-A01; B12-D03; B12-D07; B12-F02; B12-F07; **B12-G07**; B12-H02; B12-H03;

B12-K04; B12-K06; D05-H09
ABEQ US 5198424 A UPAB: 19931006
Isolated peptide with 8-118 amino acids comprises a sequence selected from:- CX1X2X3YTX4LVAIQNKX5E,
CX1X2H2YTX4LVAIQ
YTX4LVAIQNKX5E,
X2X3YTX4LVAIQ,
X3YTX4LVAIQ,
YTX4LVAIQ
RKX6X7X8X9WX10WV.GTX11KX12LTX13E,
RKX6X7X8X9WX10WV,
X11KX12LTX13EAX14NWX15X16,
AX14NWX15X16X7EPNNX17X18X19X20ED,
AX14NWX15X16X7EPNN,
AX14NWX15X16X7EPNNX17X18, and
X15X16X7EPNNX17X18X19X20ED,
X1 = Q or R; X2 = N, Q or D; X3 = R or N; X4 = D or H. X5 = N, E or A; X6 = N, V or I; X7 = N or G; X8 = K, N or G. X9 = T, V or I; X10 = T or V; X11 = K, Q or N; X12 = A, P or S. X13 = N or E; X14 = E or K; X15 = A or G; X16 = D or P. X17 = K or R; X18 = R, Q or K; X19 = N or K; X20 = N, D or K.
USE/ADVANTAGE - Inhibits binding of neutrophils and monocytes to GMP-140 and is used as a prosthetic for implantation and a diagnostic. Also to modulate or inhibit coagulation or inflammatory processes.
0
ABEQ EP 544815 A UPAB: 19931115
An isolated peptide derived from the lectin-like domain of granule membrane protein 140 (GMP-14) inhibiting bindering of neutrophils and monocytes to GMP-140, the peptide may be CONRYTOLVAJQNKNE (I), AENWADNEPNNKRNNED, RKNNKTWTWVGTKKALTNE, KKALTNEAENWAD and portions of these inhibiting binding of neutrophils and monocytes to GMP-10.
Also claimed are an isolated carbohydrate binding to a **selectin**, where the carbohydrate comprises an alpha 1,3-fucosylated, alpha 2,3-sialyated lactosaminoglycan structure, the carbohydrate may be (i) sialyl Lex, difucosyl sialyl Lex or longer polyfucosylated polyacetosaminoglycans or (ii) NeuAcalpha 2, 3 Galbetal, 4 (Fuc alpha 1,3)GlcNAc beta1-R, where R is a protein or other carbohydrate structure, (C) a method for modulating an inflammatory response, (D) an antibody to an isolated carbohydrate binding to a **selectin**, (**E**) an isolated protein component of a ligand for **selectins**
.
USE/ADVANTAGE - The peptides, carbohydrates structures and antibodies can be used for the detection of human disorders in which GMP-140 or GMP-140 ligands may be defective. They can also be used in the modulation or inhibition of coagulation processes or inflammatory processes e.g. in the treatment of injury from ischaemia and reperfusion, bacterial sepsis and disseminated intravascular coagulation, adult respiratory distress syndrome, tumour metastasis, rheumatoid arthritis and atherosclerosis.

L83 ANSWER 38 OF 41 WPIX (C) 2002 THOMSON DERWENT
AN 1992-064706 [08] WPIX
DNC C1992-029618
TI Clearing bioactive substances from bloodstream - comprises capturing agent which binds to bioactive substance and ligand which binds to cellular receptor.
DC B04 B05
IN SELMER, J
PA (NOVO) NOVO-NORDISK AS
CYC 25
PI WO 9201469 A 19920206 (199208)*
RW: AT BE CH DE DK ES FR GB GR IT LU NL SE
W: AU CA CS FI HU JP KR NO PL SU US
AU 9182828 A 19920218 (199222) A61K039-00 <--

EP 540588 A1 19930512 (199319) EN A61K039-00 <--
R: AT BE CH DE DK ES FR GB GR IT LI LU NL SE
FI 9300269 A 19930322 (199322) A61K000-00
NO 9300218 A 19930324 (199325) A61K039-00 <--
JP 05509092 W 19931216 (199404) 16p A61K039-395 <--
AU 659092 B 19950511 (199527) A61K047-48 <--
EP 540588 B1 19950621 (199529) EN 33p A61K039-00 <--
R: AT BE CH DE DK ES FR GB GR IT LI LU NL SE
DE 69110679 E 19950727 (199535) A61K039-00 <--

ADT AU 9182828 A AU 1991-82828 19910724, WO 1991-DK215 19910724; EP 540588 A1 EP 1991-913278 19910724, WO 1991-DK215 19910724; FI 9300269 A WO 1991-DK215 19910724, FI 1993-269 19930122; NO 9300218 A WO 1991-DK215 19910724, NO 1993-218 19930122; JP 05509092 W JP 1991-512515 19910724, WO 1991-DK215 19910724; AU 659092 B AU 1991-82828 19910724; EP 540588 B1 EP 1991-913278 19910724, WO 1991-DK215 19910724; DE 69110679 E DE 1991-610679 19910724, EP 1991-913278 19910724, WO 1991-DK215 19910724

FDT AU 9182828 A Based on WO 9201469; EP 540588 A1 Based on WO 9201469; JP 05509092 W Based on WO 9201469; AU 659092 B Previous Publ. AU 9182828, Based on WO 9201469; EP 540588 B1 Based on WO 9201469; DE 69110679 E Based on EP 540588, Based on WO 9201469

PRAI DK 1990-1762 19900724

REP 2.Jnl.Ref; EP 149709; EP 187658; EP 308208; EP 353960; JP 58103664; US 4624846; US 4863713; US 4932412; WO 8706263; WO 8905140

IC ICM **A61K039-395**
ICS A61K037-02; **A61K047-48**; A61K049-00

ICA A61K045-00

AB WO 9201469 A UPAB: 19931006
A pharmaceutical or diagnostic compsn is claimed comprising a separate containers. (a) a capturing agent capable of binding to a bioactive substance as well as to a ligand or ligand analogue which is able to bind to a cellular receptor and (b) a ligand or ligand analogue capable to binding to a cellular receptor as well as to the capturing agent. The capturing agent may be monofunctional and may comprise an antibody or a cellular receptor or may be bifunctional and may comprise. (a) a bispecific antibody, (b) a conjugate of an antibody and a cellular receptor (other than the specific ligand-binding receptor) or a fragment comprising the binding side for the bioactive substance, a single-stranded.oligonucleotide an **intercellular adhesion molecule** or a complexing agent (e.g. biotin, avidin, lectin or a drug) or (c) a conjugate of a cellular receptor (other than the specific ligand-binding receptor) or a fragment comprising the binding site for the bioactive substance and a single-stranded oligonucleotide, an **intercellular adhesion molecule** or a complexing agent (e.g. biotin, avidin, lectin or a drug). USE/ADVANTAGE- The compsns. provide for the rapid clearance of bioactive substances from the blood circulation.
0/9

FS CPI

FA AB; DCN

MC CPI: B01-D02; B04-A01; B04-A04; B04-B02B2; B04-B02C3; B04-B04A1; B04-B04A5; B04-B04A6; **B04-B04C2**; **B04-B04C5**; B04-B04D1; B04-B04D2; B04-B04D5; B04-B04G; B04-C01A; B05-A03B; B05-A04; B06-F03; B07-D04C; B10-C03; B12-C06; B12-C10; B12-D04; B12-E07; B12-H02

ABEQ EP 540588 A UPAB: 19931113
Pharmaceutical or diagnostic compsn. comprises separate containers, (a) capturing agent capable of binding to bioactive substance as well as to ligand or ligand analogue which is able to bind to a cellular receptor and (b) ligand or ligand analogue capable to binding to a cellular receptor as well as to the capturing agent.

The capturing agent may be monofunctional and may comprise antibody or cellular receptor or may be bifunctional and may comprise (a) bispecific antibody, (b) conjugate of antibody and cellular receptor

(other than the specific ligand-binding receptor) or fragment comprising the binding side for the bioactive substance, single-stranded oligonucleotide **intercellular adhesion mol**.
or complexing agent (e.g. biotin, avidin, lectin or a drug) or (c) conjugate or a cellular receptor (other than the specific ligand-binding receptor) or a fragment comprising the binding site for the bioactive substance and single-stranded oligonucleotide, **intercellular adhesion molecule** or complexing agent (e.g. biotin, avidin, lectin or a drug).

USE/ADVANTAGE - The compsns. provide for the rapid clearance of bioactive substances from the blood circulation.

ABEQ EP 540588 B UPAB: 19950727
A pharmaceutical or diagnostic composition comprising, in separate containers, (a) a capturing agent capable of binding to a bioactive substance so as to make it possible to locate, neutralise and/or remove the bioactive substance on administration of the capturing agent; and (b) a ligand or ligand analogue capable of binding to a cellular receptor found in an organ through which waste products of the body are usually eliminated, the capturing agent being provided with means to bind the ligand or ligand analogue, or the ligand or ligand analogue being provided with means to bind the capturing agent, or both the capturing agent and the ligand analogue being provided with complementary binding means.
Dwg.0/9

L83 ANSWER 39 OF 41 WPIX (C) 2002 THOMSON DERWENT
AN 1992-024187 [03] WPIX
CR 1992-024188 [03]; 1997-019866 [02]; 1998-311449 [27]
DNC C1992-010420
TI New **selectin** binding oligosaccharide ligands for pharmaceuticals - inhibit inflammatory disease **e**.g. asthma, psoriasis and are used in diagnosis in liposome(s).
DC B04 B07
IN GAETA, F C; PAULSON, J C; PEREZ, M S; RATCLIFFE, R M; GAETA, F C A; PHILLIPS, M L; THOMSON, D S
PA (CYTE-N) CYTEL CORP
CYC 39
PI WO 9119501 A 19911226 (199203)* 101p
RW: AT BE CH DE DK ES FR GB GR IT LI LU MC MW NL OA SD SE
W: AU BB BG BR CA FI HU JP KP KR LK MG NO PL RO SU
AU 9180077 A 19920107 (199217)
AU 9181029 A 19920107 (199217)
ZA 9104557 A 19920325 (199218) 102p
EP 533834 A1 19930331 (199313) EN A61K031-70
R: AT BE CH DE DK ES FR GB GR IT LI LU NL SE
NO 9204830 A 19930208 (199318) A61K031-70
JP 05507923 W 19931111 (199350) 29p A61K045-00
NZ 238556 A 19940126 (199407) C08L005-00
SG 52563 A1 19980928 (199903) A61K031-70
IL 98493 A 19981206 (199913) A61K031-73
RU 2123338 C1 19981220 (200017) A61K031-70
ADT ZA 9104557 A ZA 1991-4557 19910614; EP 533834 A1 EP 1991-912402 19910614, WO 1991-US4284 19910614; NO 9204830 A WO 1991-US4284 19910614, NO 1992-4830 19921214; JP 05507923 W JP 1991-510983 19910522, WO 1991-US3592 19910522; NZ 238556 A NZ 1991-238556 19910614; SG 52563 A1 SG 1996-6092 19910614; IL 98493 A IL 1991-98493 19910613; RU 2123338 C1 RU 1992-16522 19910614
FDT EP 533834 A1 Based on WO 9119502; JP 05507923 W Based on WO 9119501
PRAI US 1990-632390 19901221; US 1990-538853 19900615; US 1990-619319 19901128
REP 14Jnl.Ref; 8.Jnl.Ref
IC ICM A61K031-70; A61K031-73; A61K045-00; C08L005-00
ICS A61K031-715; A61K035-66; A61K037-02; A61K037-20; A61K038-03; **A61K039-00**; **A61K047-48**; G01N033-566

ICA C07H003-06
AB WO 9119501 A UPAB: 20000405
Compsns. contain, apart from a **carrier**, (a) a cpd. (I) contg. a selectin-binding oligosaccharide residue (OR) or (b) an immunoglobulin (Ig) to bind selectively an oligosaccharide ligand (Li) recognised by a selectin cell-surface receptor.
USE/ADVANTAGE - Used to inhibit **selectin**-mediated intra-cellular adhesion of inflammatory disease (**e**.g, reperfusion injury, asthma, psoriasis, septic shock or nephritis) or metastasis. Also used, **e**.g, when included in liposomes, to target other therapeutic agents or when labelled for diagnostic in vitro imaging. Admin. intravenously, orally or as an aerosol, pref. at a daily dose of 5-200 mg (I).
FS CPI
FA AB; DCN
MC CPI: B04-B01B; B04-B04A6; **B04-B04C6**; B04-C02; B12-A01; B12-A07; B12-D02; B12-D07; B12-D10; B12-G03; **B12-G07**; B12-K02; B12-K04C; B12-M11F

L83 ANSWER 40 OF 41 WPIX (C) 2002 THOMSON DERWENT
AN 1991-132635 [18] WPIX
DNC C1991-057184
TI Compsns. disrupting endothelial and epithelial cell junctions - contg. agent reactive with cell-bound adhesion mol. to enhance blood-brain transfer.
DC B04 D16
IN LIAW, C W; RUBIN, L L; TOMASELLI, K J
PA (ATHE-N) ATHENA NEUROSCIENCES INC; (ATHE-N) ATHENA NEUROSCIENCE INC; (ATHE-N) ATHENA NEUROSCIENCE
CYC 15
PI WO 9104745 A 19910418 (199118)*
RW: AT BE CH DE DK ES FR GB IT LU NL SE
W: CA JP
EP 494175 A1 19920715 (199229) EN 72p A61K037-02
R: AT BE CH DE DK ES FR GB IT LI LU NL SE
JP 05500504 W 19930204 (199310) 24p A61K047-46 <--
EP 494175 A4 19930505 (199526)
ADT EP 494175 A1 EP 1990-913684 19900913, WO 1990-US5105 19900913; JP 05500504 W JP 1990-512779 19900913, WO 1990-US5105 19900913; EP 494175 A4 EP 1990-913684
FDT EP 494175 A1 Based on WO 9104745; JP 05500504 W Based on WO 9104745
PRAI US 1989-413332 19890927; US 1990-571267 19900823
REP 5.Jnl.Ref; US 4671958; 1.Jnl.Ref; WO 8904663
IC ICM A61K037-02; **A61K047-46**
ICS **A61K039-395**; C07K007-08; C07K007-10; C07K013-00; C07K015-28
AB WO 9104745 A UPAB: 19930928
Compsn. for opening tight junctions between microvascular endothelial cells is claimed, where the drug can cross the permeability barrier imposed by junctions. Compsn. contains an agent reactive with type(s) of cell-bound **cell adhesion molecule** which would otherwise mediate tight junction formation between microvascular endothelial cells, so cell-cell adhesion is disrupted.
The **cell adhesion molecule** is related to a cadherin selected from E-, N- and P-cadherin. The agent is an inhibitor of the binding to cells of the **cell adhesion molecule**, with a sequence, e.g., NH2-YILYSHAVSSNGNAVED-CONH2. Also claimed is a drug delivery compsn. comprising the conjugate of a drug and the agent.
USE/ADVANTAGE - **Cell adhesion molecule** is from the HAV region of E-cadherin and these open tight junctions of brain endothelial cell blood-brain barriers and of epithelial cells forming junctions. The drug administered may be nerve growth factor, anti-Parkinsonism drugs and brain enzymes known to be missing in

sphingolipidoses, e.g., Tay-Sachs disease. The compsn. may also be used with antibiotics to treat retinal infections.
0/9

FS CPI
FA AB
MC CPI: B02-Z; B04-B02C; B04-B04J; B11-C03; B12-C04; B12-F07; B12-G04; **B12-L04**; B12-M05; D05-H10

L83 ANSWER 41 OF 41 WPIX (C) 2002 THOMSON DERWENT
AN 1990-108987 [15] WPIX
CR 1992-034055 [05]; 1997-558201 [51]; 1999-166572 [14]; 2000-248047 [22]; 2000-571334 [53]; 2001-023396 [03]; 2002-105208 [14]
DNC C1990-047807
TI Human rhinovirus major receptor prepn. - comprises detergent-complexed glyco-protein used to inhibit infectivity of virus.
DC B04 D16
IN DAVIS, G; GREVE, J; MCCELLAND, A; GREVE, J M; MCCLELLAND, A
PA (MOLE-N) MOLECULAR THERAPEUTICS INC; (FARB) BAYER CORP; (MILE) MILES INC
CYC 24
PI EP 362531 A 19900411 (199015)* 15p
R: AT BE CH DE ES FR GB GR IT LI LU NL SE
PT 91570 A 19900330 (199017)
NO 8903373 A 19900326 (199018)
AU 8940271 A 19900308 (199019)
DK 8904312 A 19900302 (199021)
FI 8904065 A 19900302 (199022)
ZA 8906668 A 19900627 (199030)
JP 02238892 A 19900921 (199044)
NZ 230474 A 19930326 (199316) C07K015-04
AU 637324 B 19930527 (199328) C07K013-00
IL 91454 A 19950831 (199543) A61K038-17
US 5589453 A 19961231 (199707) 9p A61K038-17
CA 1339193 C 19970805 (199743) A61K038-17
EP 362531 B1 19991110 (199952) EN C07K014-705
R: AT BE CH DE ES FR GB GR IT LI LU NL SE
DE 68929096 E 19991216 (200005) C07K014-705
ES 2141076 T3 20000316 (200021) C07K014-705
US 6051231 A 20000418 (200026) A61K038-00
JP 3253064 B2 20020204 (200211) 17p C07K014-705
DK 174095 B 20020610 (200245) A61K038-17
ADT EP 362531 A EP 1989-115358 19890819; ZA 8906668 A ZA 1989-6668 19890831; JP 02238892 A JP 1989-227301 19890901; NZ 230474 A NZ 1989-230474 19890829; AU 637324 B AU 1989-40271 19890825; IL 91454 A IL 1989-91454 19890828; US 5589453 A Cont of US 1988-239571 19880901, Cont of US 1993-14087 19930204, Cont of US 1993-139622 19931019, US 1994-316383 19940930; CA 1339193 C CA 1989-609473 19890825; EP 362531 B1 EP 1989-115358 19890819; DE 68929096 E DE 1989-629096 19890819, EP 1989-115358 19890819; ES 2141076 T3 EP 1989-115358 19890819; US 6051231 A CIP of US 1988-239571 19880901, Cont of US 1988-262428 19881025, Cont of US 1993-7049 19930121, Cont of US 1993-139621 19931019, US 1994-316382 19940930; JP 3253064 B2 JP 1989-227301 19890901; DK 174095 B DK 1989-4312 19890831
FDT AU 637324 B Previous Publ. AU 8940271; DE 68929096 E Based on EP 362531; ES 2141076 T3 Based on EP 362531; JP 3253064 B2 Previous Publ. JP 02238892; DK 174095 B Previous Publ. DK 8904312
PRAI US 1989-390662 19890810; US 1988-239571 19880901; US 1988-262428 19881025; US 1993-14087 19930204; US 1993-139622 19931019; US 1994-316383 19940930; US 1993-7049 19930121; US 1993-139621 19931019; US 1994-316382 19940930
REP 5.Jnl.Ref; EP 169146; EP 289949; EP 319815
IC ICM A61K038-00; A61K038-17; C07K013-00; C07K015-04
ICS A61K037-02; A61K038-16; **A61K039-00**; **A61K039-125**; **A61K039-14**; **A61K047-48**; A61P011-02; A61P031-14;

A61P031-16; C07K003-02; C07K003-12; C07K015-06; C07K015-14; C12N015-09; C12P021-00; C12P021-02
ICA C07K014-705
ICI C12P021-02, C12R001:91
AB EP 362531 A UPAB: 20020717
Water soluble human rhinovirus (HRV) major receptor prepn. comprises detergent-complexed glycoprotein isolated from animal cells that express the HRV major receptor and which exhibits the ability to bind to HRV capsids and reduce infectivity of the virus.

Also claimed is a HRV receptor protein selected from biologically active receptor protein fragments, functional domains and analogues, which exhibits the ability to bind to HRV capsid of the major receptor class and inhibits infectivity of the virus.

USE/ADVANTAGE - The receptor prepn. can be administered in vivo to those areas of the body susceptible to infection by HRV, eg. by intranasal spray, to inhibit the initiation or the spread of HRV infections. The HRV receptor protein (HRR) was found to be the same as **Intercellular Adhesion Molecule-1** (**ICAM-1**) and could be used for disrupting interactions between **ICAM** and LFA-1 which could be used for the treatment of inflammation.

Dwg.0/2
FS CPI
FA AB
MC CPI: B04-B04A6; B12-A06; B12-D07; D05-H08
ABEQ US 5589453 A UPAB: 19970212
A method for reducing the infection by human rhinovirus (HRV) of a host cell susceptible to infection by HRV, comprising contacting the virus under conditions favourable for binding with an antiviral agent selected from the group consisting of human rhinovirus major receptor protein (HRR) and fragments thereof in a form that exhibits the ability to bind to HRV capsids and reduce infectivity of the virus.

Dwg.0/0

=> fil medline
FILE 'MEDLINE' ENTERED AT 13:36:35 ON 15 AUG 2002

FILE LAST UPDATED: 14 AUG 2002 (20020814/UP). FILE COVERS 1958 TO DATE.

On June 9, 2002, MEDLINE was reloaded. See HELP RLOAD for details.

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=> d all tot

L103 ANSWER 1 OF 13 MEDLINE
AN **2002132772** MEDLINE
DN **21824052** PubMed ID: **11835199**
TI Targeting of liposomes to melanoma cells with high levels of **ICAM -1** expression through adhesive peptides from immunoglobulin domains.
AU Jaafari M R; Foldvari M
CS College of Pharmacy and Nutrition University of Saskatchewan, 110 Science Place, Saskatoon, SK, Canada, S7N 5C9.
SO JOURNAL OF PHARMACEUTICAL SCIENCES, (2002 Feb) 91 (2) 396-404.
Journal code: 2985195R. ISSN: 0022-3549.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)

LA English
FS Priority Journals
EM 200204
ED Entered STN: 20020301
Last Updated on STN: 20020420
Entered Medline: 20020419
AB The P(0) protein is an immunoglobulin [Ig] superfamily **cell adhesion molecule** from peripheral nerve myelin. Synthetic peptides derived from the P(0) protein and leukocyte function-associated antigen-1 (LFA-1) were investigated as potential ligands for targeting liposomes to **intercellular adhesion molecule-1 (ICAM-1**) expressing melanoma cells. Three synthetic P(0) peptides and one LFA-1 peptide were selected for linkage to liposome surfaces. P(0)-peptide-1, from the extracellular Ig-like domain, increased liposome binding to M21 (6.36-fold) and A-375 (1.85-fold) cells compared to control blank liposomes, but did not increase liposome binding to MeM 50-10 cells. P(0)-peptide-3, from the basic intracellular domain, increased binding of liposomes to all three melanoma cell lines nonspecifically due to its high content of positively charged amino acids. LFA-1- and negative control arg-gly-asp (RGD)-peptides did not affect liposome binding to M21 cells. The extent of P(0)-peptide-1-liposome binding to human melanoma cell lines correlated with the level of cellular **ICAM-1** expression (r(2) = 0.868). P(0)-peptide-1-mediated targeting of liposomes might, therefore, prove useful in the development of drug delivery systems for treatment of **ICAM-1** expressing malignant melanomas.
 J Pharm Sci 91:396-404, 2002
CT Check Tags: Human
***Drug Delivery Systems: MT, methods**
***Immunoglobulins: ME, metabolism**
Immunoglobulins: PD, pharmacology
***Intercellular Adhesion Molecule-1: BI, biosynthesis**
Ligands
***Liposomes: ME, metabolism**
Liposomes: PD, pharmacology
Melanoma: DT, drug therapy
***Melanoma: ME, metabolism**
*Peptides: ME, metabolism
Peptides: PD, pharmacology
Protein Binding
Tumor Cells, Cultured
RN **126547-89-5 (Intercellular Adhesion Molecule-1)**
CN 0 (Immunoglobulins); 0 (Ligands); 0 (Liposomes); 0 (Peptides)

L103 ANSWER 2 OF 13 MEDLINE
AN **2001293763** MEDLINE
DN **21250700** PubMed ID: **11352731**
TI Polymerized liposome assemblies: bifunctional macromolecular selectin inhibitors mimicking physiological selectin ligands.
AU Bruehl R E; Dasgupta F; Katsumoto T R; Tan J H; Bertozzi C R; Spevak W; Ahn D J; Rosen S D; Nagy J O
CS Department of Anatomy and Program in Biomedical Sciences, University of California, San Francisco, California 94143, USA.
NC R4 AI 43789A (NIAID)
SO BIOCHEMISTRY, (2001 May 22) 40 (20) 5964-74.
Journal code: 0370623. ISSN: 0006-2960.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 200108

ED Entered STN: 20010820
Last Updated on STN: 20010820
Entered Medline: 20010816

AB Monomeric sialyl Lewis(X) (sLe(x)) and sLe(x)-like oligosaccharides are minimal structures capable of supporting **selectin** binding in vitro. However, their weak binding interactions do not correlate with the high-affinity binding interactions witnessed in vivo. The polyvalent display of carbohydrate groups found on cell surface glycoprotein structures may contribute to the enhanced binding strength of **selectin**-mediated adhesion. Detailed biochemical analyses of physiological **selectin** ligands have revealed a complicated composition of molecules that bind to the **selectins** in vivo and suggest that there are other requirements for tight binding beyond simple carbohydrate multimerization. In an effort to mimic the high-affinity binding, polyvalent scaffolds that contain multicomponent displays of **selectin**-binding ligands have been synthesized. Here, we demonstrate that the presentation of additional anionic functional groups in the form of sulfate esters, on a polymerized liposome surface containing a multimeric array of sLe(x)-like oligosaccharides, generates a highly potent, bifunctional macromolecular assembly. This assembly inhibits L-, **E-**, and **P-selectin** binding to GlyCAM-1, a physiological ligand better than sLe(x)-like liposomes without additional anionic charge. These multivalent arrays are 4 orders of magnitude better than the monovalent carbohydrate. Liposomes displaying 3'-sulfo Lewis(X)-like oligosaccharides, on the other hand, show slight loss of binding with introduction of additional anionic functional groups for **E-** and **P-selectin** and negligible change for L-**selectin**. The ability to rapidly and systematically vary the composition of these assemblies is a distinguishing feature of this methodology and may be applied to the study of other systems where composite binding determinants are important for high-affinity binding.

CT Check Tags: Human; Support, U.S. Gov't, Non-P.H.S.; Support, U.S. Gov't, P.H.S.
Binding, Competitive
Biopolymers: CH, chemistry
Biopolymers: ME, metabolism
Biopolymers: PH, physiology
E-Selectin: ME, metabolism
Inhibitory Concentration 50
L-Selectin: ME, metabolism
Lewis Blood-Group System: CH, chemistry
Lewis Blood-Group System: ME, metabolism
Lewis Blood-Group System: PH, physiology
Ligands
Liposomes: CS, chemical synthesis
***Liposomes: ME, metabolism**
***Liposomes: PD, pharmacology**
*Molecular Mimicry
Mucins: ME, metabolism
Mucins: PH, physiology
Oligosaccharides: CS, chemical synthesis
Oligosaccharides: ME, metabolism
Oligosaccharides: PD, pharmacology
P-Selectin: ME, metabolism
Protein Binding
***Selectins: ME, metabolism**

RN **126880-86-2 (L-Selectin)**; 145895-89-2 (sulfated glycoprotein p50)

CN 0 (5-acetylneuraminyl-(2-3)-galactosyl-(1-4)-(fucopyranosyl-(1-3))-N-acetylglucosamine); 0 (Biopolymers); **0 (E-Selectin)**; 0 (Lewis Blood-Group System); 0 (Ligands); 0 (Liposomes); 0 (Mucins); 0 (Oligosaccharides); **0 (P-Selectin)**; **0 (Selectins)**

L103 ANSWER 3 OF 13 MEDLINE
AN **2001152160** MEDLINE
DN **21121489** PubMed ID: **11229813**
TI Sialyl Lewis(x)-liposomes as vehicles for site-directed, **E-selectin**-mediated drug transfer into activated endothelial cells.
AU Stahn R; Grittner C; Zeisig R; Karsten U; Felix S B; Wenzel K
CS Max Delbruck Center for Molecular Medicine, Berlin, Germany.. renate.stahn@nemod.com
SO CELLULAR AND MOLECULAR LIFE SCIENCES, (2001 Jan) 58 (1) 141-7. Journal code: 9705402. ISSN: 1420-682X.
CY Switzerland
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 200103
ED Entered STN: 20010404
Last Updated on STN: 20010404
Entered Medline: 20010315
AB **E-selectin**, exclusively expressed on activated endothelial cells, is a potential target for site-directed delivery of agents. We and others have shown that sialyl LewisX-liposomes (sLe(x)-liposomes) are recognized by **E-selectin**. We now report an approach employing sLe(x)-liposomes to deliver antisense oligonucleotides (AS-ODNs) directed against the adhesion molecule **ICAM-1** to activated vascular endothelial cells. **ICAM-1** expression was analyzed at the protein level by immunofluorescence and a cell surface ELISA, and at the RNA level by RT-PCR. We have investigated two different AS-ODNs complementary to the 3' untranslated region and the AUG translation initiation codon of **ICAM-1** mRNA. Both inhibited protein expression, but did not influence the mRNA level, pointing to a hybridization of AS-ODNs with the mRNA in the cytoplasm. Our results demonstrate the feasibility of a novel approach for the delivery of agents to activated endothelial cells by glycoliposomes targeted to **E-selectin**.
CT Check Tags: Human; Support, Non-U.S. Gov't
Cells, Cultured
Codon, Initiator: GE, genetics
Dose-Response Relationship, Drug
Down-Regulation: DE, drug effects
***Drug Delivery Systems: MT, methods**
E-Selectin: GE, genetics
***E-Selectin: ME, metabolism**
Endothelium, Vascular: CY, cytology
*Endothelium, Vascular: ME, metabolism
Enzyme-Linked Immunosorbent Assay
Fluorescent Antibody Technique
Intercellular Adhesion Molecule-1: BI, biosynthesis
Intercellular Adhesion Molecule-1: GE, genetics
***Liposomes: CH, chemistry**
***Liposomes: ME, metabolism**
Oligonucleotides, Antisense: AD, administration & dosage
Oligonucleotides, Antisense: GE, genetics
Oligonucleotides, Antisense: PD, pharmacology
*Oligosaccharides: ME, metabolism
Organ Specificity
Protein Binding
RNA, Messenger: GE, genetics
RNA, Messenger: ME, metabolism
Reverse Transcriptase Polymerase Chain Reaction
RN **126547-89-5 (Intercellular Adhesion Molecule-1)**
CN 0 (5-acetylneuraminyl-(2-3)-galactosyl-(1-4)-(fucopyranosyl-(1-3))-N-acetylglucosamine); 0 (Codon, Initiator); **0 (E-Selectin)**; 0 (Liposomes); 0 (Oligonucleotides, Antisense); 0 (Oligosaccharides); 0

(RNA, Messenger)

L103 ANSWER 4 OF 13 MEDLINE
AN **2001081197** MEDLINE
DN **20530337** PubMed ID: **11077218**
TI Gene therapy of transplant arteriopathy by liposome-mediated transfection of endothelial nitric oxide synthase.
AU Iwata A; Sai S; Moore M; Nyhuis J; de Fries-Hallstrand R; Quetingco G C; Allen M D
CS Division of Cardiothoracic Surgery, University of Washington, Seattle, Washington 98104, USA.. aiwata@u.washington.edu
SO JOURNAL OF HEART AND LUNG TRANSPLANTATION, (2000 Nov) 19 (11) 1017-28. Journal code: 9102703. ISSN: 1053-2498.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 200101
ED Entered STN: 20010322
Last Updated on STN: 20010322
Entered Medline: 20010111
AB BACKGROUND: Transplant arteriopathy is the major factor limiting long-term survival after cardiac transplantation. We have previously demonstrated that liposome-mediated gene delivery of endothelial nitric oxide synthase (eNOS) to donor hearts reduces ischemia-reperfusion injury by blocking NFkappaB activation, adhesion molecule expression, and leukocyte infiltration. In this study, we used gene transfer of eNOS in a rabbit carotid transplant model to see whether these same effects would similarly ameliorate transplant arteriopathy. METHODS: Liposomes complexed to the gene encoding eNOS were injected into donor carotid arterial segments that were transplanted orthotopically into recipient carotid arteries (n = 10). Controls included transplanted carotids transfected with liposomes complexed to empty plasmids (no functional gene) (n = 4) and transplanted carotids treated with saline (n = 6). Transplanted arteries were harvested for processing at 21 days. Intima/media (I/M) area ratios were calculated by computerized image analysis. Infiltrating T-lymphocytes and macrophages, and expression of **VCAM-1** and **ICAM-1** were quantified on immunocytochemistry. RESULTS: The I/M ratio was significantly reduced in eNOS-transfected arteries compared with arteries transfected with empty plasmids and saline-treated controls. Compared to transplanted control arteries, eNOS-transfected arteries demonstrated significantly reduced T-cell infiltration into the intima and significantly reduced macrophage infiltration into the media. Cell surface expression of **VCAM-1** and **ICAM-1** were both reduced in eNOS-transfected arteries. CONCLUSIONS: ENOS gene delivery can suppress neointimal lesion formation and T-lymphocyte and macrophage infiltration in transplanted arteries, associated with a reduction in relevant adhesion molecule expression. Thus, gene therapy with eNOS may not only reduce ischemia-reperfusion injury but may also ameliorate transplant arteriopathy in transplanted hearts.
CT Check Tags: Animal; Human; Support, Non-U.S. Gov't
Carotid Arteries: DE, drug effects
Carotid Arteries: PA, pathology
Carotid Arteries: TR, transplantation
Disease Models, Animal
*Endothelium, Vascular: EN, enzymology
Endothelium, Vascular: PA, pathology
Gene Expression: PH, physiology
*Gene Therapy
*Heart Transplantation
Intercellular Adhesion Molecule-1: ME, metabolism
Liposomes
Macrophages: PA, pathology

Myocardial Reperfusion Injury: PA, pathology
*Myocardial Reperfusion Injury: TH, therapy
Nitric-Oxide Synthase: AD, administration & dosage
*Nitric-Oxide Synthase: GE, genetics
Rabbits
T-Lymphocytes: PA, pathology
*Transfection
Tunica Intima: DE, drug effects
Tunica Intima: PA, pathology
Tunica Media: DE, drug effects
Tunica Media: PA, pathology
Vascular Cell Adhesion Molecule-1: ME, metabolism
RN **126547-89-5 (Intercellular Adhesion Molecule-1)**
CN 0 (Liposomes); **0 (Vascular Cell Adhesion Molecule-1)**; EC 1.14.13.39 (Nitric-Oxide Synthase)

L103 ANSWER 5 OF 13 MEDLINE
AN **2000249019** MEDLINE
DN **20249019** PubMed ID: **10785601**
TI Antitumour activity of cytotoxic liposomes equipped with selectin ligand SiaLe(X), in a mouse mammary adenocarcinoma model.
AU Vodovozova E L; Moiseeva E V; Grechko G K; Gayenko G P; Nifant'ev N E; Bovin N V; Molotkovsky J G
CS Shemyakin-Ovchinnikov Institute of Bioorganic Chemistry, Russian Academy of Sciences, ul. Miklukho-Maklaya 16/10, Moscow, Russia.
SO EUROPEAN JOURNAL OF CANCER, (2000 May) 36 (7) 942-9.
Journal code: 9005373. ISSN: 0959-8049.
CY ENGLAND: United Kingdom
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 200007
ED Entered STN: 20000811
Last Updated on STN: 20000811
Entered Medline: 20000728
AB The overexpression of lectins by malignant cells compared with normal ones can be used for the targeting of drug-loaded liposomes to tumours with the help of specific carbohydrate ligands (vectors). Recently we have shown that liposomes bearing specific lipid-anchored glycoconjugates on a polymeric matrix bind in vitro to human malignant cells more effectively and, being loaded with a lipophilic prodrug of merphalan, reveal higher cytotoxic activity compared with unvectored liposomes. In this study, carbohydrate-equipped cytotoxic liposomes were tested in vivo in a mouse breast cancer model, BLRB-Rb (8.17)1Iem strain with a high incidence of spontaneous mammary adenocarcinoma (SMA). Firstly, a cell line of the SMA was established which was then used to determine the specificity of the tumour cell lectins. After screening of the lectin specificity of a number of fluorescent carbohydrate probes, SiaLe(X) was shown to be the ligand with the most affinity, and a lipophilic vector bearing this saccharide was synthesised. Then different liposomal formulations of the synthetic merphalan lipid derivative and SiaLe(X) vector were prepared and applied in the treatment of mice with grafted adenocarcinomas. The results of the tumorigenesis data show that the therapeutic efficacy of merphalan increases sharply after its insertion as a lipophilic prodrug into the membrane of SiaLe(X)-vectored liposomes.
CT Check Tags: Animal; Female; Support, Non-U.S. Gov't
***Adenocarcinoma: DT, drug therapy**
Drug Screening Assays, Antitumor
Ligands
Liposomes: AD, administration & dosage
***Mammary Neoplasms, Experimental: DT, drug therapy**
*Melphalan: TU, therapeutic use
Mice

Selectins: AD, administration & dosage
Tumor Cells, Cultured
RN 148-82-3 (Melphalan)
CN 0 (Ligands); 0 (Liposomes); **0 (Selectins)**

L103 ANSWER 6 OF 13 MEDLINE
AN **1999337513** MEDLINE
DN **99337513** PubMed ID: **10407086**
TI Cellular uptake of liposomes targeted to **intercellular adhesion molecule-1 (ICAM-1**) on bronchial epithelial cells.
AU Mastrobattista E; Storm G; van Bloois L; Reszka R; Bloemen P G; Crommelin D J; Henricks P A
CS Department of Pharmaceutics, Utrecht Institute for Pharmaceutical Sciences, Utrecht University, P.O. Box 80.082, 3508 TB, Utrecht, The Netherlands.. e.mastrobattista@pharm.uu.nl
SO BIOCHIMICA ET BIOPHYSICA ACTA, (1999 Jul 15) 1419 (2) 353-63. Journal code: 0217513. ISSN: 0006-3002.
CY Netherlands
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199909
ED Entered STN: 19990921
Last Updated on STN: 19990921
Entered Medline: 19990903
AB Previously, it was demonstrated that immunoliposomes, bearing anti-**intercellular adhesion molecule-1** (**ICAM-1**) antibodies (mAb F10.2), can specifically bind to different cell types expressing **ICAM-1**. In this study, we have quantified the amount of immunoliposomes binding to IFN-gamma activated human bronchial epithelial cells (BEAS-2B) in vitro and studied the subsequent fate of cell-bound anti-**ICAM-1** immunoliposomes. We demonstrate that binding of the immunoliposomes to the epithelial cells depends on the liposome concentration used. After binding to the cell surface, the anti-**ICAM-1** immunoliposomes are rapidly internalised by the epithelial cells. Sixty percent of cell-bound immunoliposomes were internalised by the epithelial cells within 1 h of incubation at 37 degrees C. The results indicate that **ICAM-1** targeted immunoliposomes may be used as carriers for the intracellular delivery of anti-inflammatory drugs to sites of inflammation characterised by an increased expression of **ICAM-1**.
CT Check Tags: Human
Antibodies, Monoclonal: IM, immunology
*Bronchi: IM, immunology
Cell Adhesion
Cell Line
Drug Carriers
Epithelial Cells: IM, immunology
Epithelial Cells: ME, metabolism
Fluoresceins
Inflammation: DT, drug therapy
Inflammation: IM, immunology
***Intercellular Adhesion Molecule-1: IM, immunology**
Intercellular Adhesion Molecule-1: ME, metabolism
Interferon Type II
***Liposomes: IM, immunology**
Microscopy, Confocal
Time Factors
RN **126547-89-5 (Intercellular Adhesion Molecule-1)**; 82115-62-6 (Interferon Type II)
CN 0 (Antibodies, Monoclonal); 0 (Drug Carriers); 0 (Fluoresceins); 0

(Liposomes); 0 (calcein green)

L103 ANSWER 7 OF 13 MEDLINE
AN **1999299710** MEDLINE
DN **99299710** PubMed ID: **10370205**
TI Targetability of novel immunoliposomes prepared by a new antibody conjugation technique.
AU Bendas G; Krause A; Bakowsky U; Vogel J; Rothe U
CS Department of Pharmacy, Martin Luther University Halle, Wolfgang-Langenbeck Str. 4, D 06120, Halle, Germany.. bendas@pharmazie.uni-halle.de
SO INTERNATIONAL JOURNAL OF PHARMACEUTICS, (1999 Apr 20) 181 (1) 79-93. Journal code: 7804127. ISSN: 0378-5173.
CY Netherlands
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199907
ED Entered STN: 19990727
Last Updated on STN: 19990727
Entered Medline: 19990709
AB In order to develop long-circulating immunoliposomes (IL), which combine sterical stabilization with a superior targetability, we have introduced a new methodology for attaching monoclonal antibodies directly onto the distal ends of liposome-grafted polyethylene glycol (PEG) chains. Therefore, we have synthesized a new PEG-PE derivative, which had been endgroup-functionalized with cyanuric chloride. Antibodies can simply be coupled to this membrane anchor in mild basic conditions (pH 8.8) without the need for previous antibody derivatizations. The coupling results have been determined with consideration to various liposome parameters and have been compared to several established antibody coupling procedures, where antibodies had been linked directly to the liposome surface in the presence of PEG (conventional IL). To investigate the targetability of the resulting new IL, anti **E-selectin** mAb have been coupled and the degree of binding **selectin**-containing cells has been analyzed. The terminal coupled antibodies show a 1.8-fold higher degree of in vitro cell binding compared to conventional IL, which has been attributed to the antibody position being more easy accessible at the PEG termini. Furthermore, we have illustrated the liposome surface topology and the coupled antibodies by atomic force microscopy, which for such fluid IL has been used first. These images have finely corresponded to the cell binding results, and have been discussed in terms of antibody position and flexibility at the liposome surface. Copyright
CT Check Tags: Animal; Comparative Study; Human; Support, Non-U.S. Gov't
***Antibodies, Monoclonal: CH, chemistry**
***Antibodies, Monoclonal: ME, metabolism**
CHO Cells
Cross-Linking Reagents: CH, chemistry
Cross-Linking Reagents: ME, metabolism
***Drug Delivery Systems: MT, methods**
Drug Stability
E-Selectin: GE, genetics
E-Selectin: ME, metabolism
Hamsters
***Immunoconjugates: CH, chemistry**
***Immunoconjugates: ME, metabolism**
***Liposomes: CH, chemistry**
***Liposomes: ME, metabolism**
Microscopy, Atomic Force
Phosphatidylethanolamines: CH, chemistry
Phosphatidylethanolamines: ME, metabolism
Polyethylene Glycols: CH, chemistry
Polyethylene Glycols: ME, metabolism

Rats
Transfection
Triazines: CH, chemistry
Triazines: ME, metabolism
RN 108-77-0 (cyanuric chloride); 3026-45-7 (1,2-dipalmitoyl-3-phosphatidylethanolamine)
CN 0 (Antibodies, Monoclonal); 0 (Cross-Linking Reagents); 0 (DPPE-PGE2000); **0 (E-Selectin)**; 0 (Immunoconjugates); 0 (Liposomes); 0 (Phosphatidylethanolamines); 0 (Polyethylene Glycols); 0 (Triazines)

L103 ANSWER 8 OF 13 MEDLINE
AN **1999178577** MEDLINE
DN **99178577** PubMed ID: **10080492**
TI In vivo targeting of acoustically reflective liposomes for intravascular and transvascular ultrasonic enhancement.
AU Demos S M; Alkan-Onyuksel H; Kane B J; Ramani K; Nagaraj A; Greene R; Klegerman M; McPherson D D
CS Department of Bioengineering, University of Illinois/Chicago, USA.. d.mcpherson@nwu.edu
NC HL-46550 (NHLBI)
SO JOURNAL OF THE AMERICAN COLLEGE OF CARDIOLOGY, (1999 Mar) 33 (3) 867-75. Journal code: 8301365. ISSN: 0735-1097.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Abridged Index Medicus Journals; Priority Journals
EM 199903
ED Entered STN: 19990413
Last Updated on STN: 19990413
Entered Medline: 19990330
AB OBJECTIVES: The purpose of this study was to target acoustically reflective liposomes to atherosclerotic plaques in vivo for ultrasound image enhancement. BACKGROUND: We have previously demonstrated the development of acoustically reflective liposomes that can be conjugated for site-specific acoustic enhancement. This study evaluates the ability of liposomes coupled to antibodies specific for different components of atherosclerotic plaques and thrombi to target and enhance ultrasonic images in vivo. METHODS: Liposomes were prepared with phospholipids and cholesterol using a dehydration/ rehydration method. Antibodies were thiolated for liposome conjugation with N-succinimidyl 3-(2-pyridyldithio) propionate resulting in a thioether linkage between the protein and the phospholipid. Liposomes were conjugated to antifibrinogen or anti-**intercellular adhesion molecule-1** (anti-**ICAM-1**). In a Yucatan miniswine model, atherosclerosis was developed by crush injury of one carotid and one femoral artery and ingestion of a hypercholesterolemic diet. After full plaque development the arteries were imaged (20-MHz intravascular ultrasound catheter and 7.5-MHz transvascular linear probe) after injection of saline, unconjugated liposomes and antibody conjugated liposomes. RESULTS: Conjugated liposomes retained their acoustically reflective properties and provided ultrasonic image enhancement of their targeted structures. Liposomes conjugated to antifibrinogen attached to thrombi and fibrous portions of the atheroma, whereas liposomes conjugated to anti-**ICAM-1** attached to early atheroma. CONCLUSIONS: Our data demonstrate that this novel acoustic agent can provide varying targeting with different antibodies with retention of intravascular and transvascular acoustic properties.
CT Check Tags: Animal; Comparative Study; Support, Non-U.S. Gov't; Support, U.S. Gov't, P.H.S.
Antibodies: AD, administration & dosage
***Antibodies: DU, diagnostic use**
Arteriosclerosis: CO, complications
*Arteriosclerosis: US, ultrasonography

Carotid Arteries: US, ultrasonography
Drug Carriers
Endothelium, Vascular: ME, metabolism
Endothelium, Vascular: US, ultrasonography
Femoral Artery: US, ultrasonography
Fibrinogen: IM, immunology
*Image Enhancement
Injections, Intra-Arterial
Intercellular Adhesion Molecule-1: IM, immunology
Liposomes: AD, administration & dosage
Liposomes: CH, chemistry
***Liposomes: DU, diagnostic use**
Swine
Swine, Miniature
Thromboembolism: ET, etiology
Thromboembolism: US, ultrasonography
*Ultrasonography, Interventional: MT, methods
Video Recording
RN **126547-89-5 (Intercellular Adhesion Molecule-1)**; 9001-32-5 (Fibrinogen)
CN 0 (Antibodies); 0 (Drug Carriers); 0 (Liposomes)

L103 ANSWER 9 OF 13 MEDLINE
AN **1998455002** MEDLINE
DN **98455002** PubMed ID: **9783681**
TI In vitro targeting of acoustically reflective immunoliposomes to fibrin under various flow conditions.
AU Demos S M; Dagar S; Klegerman M; Nagaraj A; McPherson D D; Onyuksel H
CS Department of Bioengineering, University of Illinois at Chicago, USA.
NC HL-46550 (NHLBI)
SO JOURNAL OF DRUG TARGETING, (1998) 5 (6) 507-18.
Journal code: 9312476. ISSN: 1061-186X.
CY Switzerland
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199812
ED Entered STN: 19990115
Last Updated on STN: 19990115
Entered Medline: 19981223
AB We have previously demonstrated the development of acoustically reflective liposomes as a novel ultrasound contrast agent, that can be conjugated to antibodies for site specific acoustic enhancement of pathologically altered vascular tissue. The liposomes are echogenic due to the lipid composition, without gas entrapment, and have a size of less than one micron (Alkan-Onyuksel et al., 1996). When conjugated to anti-fibrinogen antibodies, the liposomes have the ability to attach to fibrin coated surfaces and thrombi in vitro as demonstrated by scanning electron microscopy and ultrasound imaging (Demos et al., 1997a). Anti-fibrinogen liposomes were shown to attach to fibrous atheroma and thrombi in a Yucatan miniswine model of induced atherosclerosis whereas liposomes conjugated to anti-**intercellular adhesion molecule-1** (anti-**ICAM-1**) were demonstrated to target early stage atherosclerotic plaques (Demos et al., 1997b). The purpose of this study is to evaluate the binding characteristics of anti-fibrinogen liposomes in vitro under a variety of flow conditions in order to optimize the targeting ability of the immunoliposomes. Radiolabeled anti-fibrinogen liposomes were applied to fibrin coated filter paper and placed in a flow circuit under controlled flow conditions. Flow conditions were altered to study the effects of different shear stresses, temperature, plasma flow and pulsatile flow on the retention of liposomes to fibrin after set time periods. The retention of liposomes conjugated to polyclonal and monoclonal antibodies as well as

Fab fragments made from monoclonal antibodies were compared. The binding characteristics of liposomes conjugated to different quantities of polyclonal antibodies were analyzed. At physiological shear stress of 1.5 N/m2 (15 dynes/cm2) over 70% of the liposomes remained attached to fibrin after two hours. A smaller and greater portion of the liposomes remained attached at higher and lower shear stresses respectively. Plasma components and temperature had no effect on liposomal retention whereas pulsatile flow resulted in a slight reduction in binding. Monoclonal antibodies showed a slight trend of reduced retention to fibrin over time as compared with polyclonal antibodies and Fab fragments. The quantity of antibody conjugated to the liposomes plays a role in liposome retention as demonstrated by the reduction in liposome retention caused by reducing the quantity of antibody conjugated to the liposomes. Anti-fibrinogen liposomes were retained to the fibrin surface to a large extent under all flow conditions likely to occur in vivo and therefore can provide site specific ultrasound contrast for a long enough time period to allow for imaging after injection.

CT Check Tags: Human; Support, Non-U.S. Gov't; Support, U.S. Gov't, P.H.S.
Acoustics
Antibodies: ME, metabolism
*Contrast Media
*Fibrin: ME, metabolism
Fibrinolysis
Heat
***Liposomes**
Stress, Mechanical
RN 9001-31-4 (Fibrin)
CN 0 (Antibodies); 0 (Contrast Media); 0 (Liposomes)

L103 ANSWER 10 OF 13 MEDLINE
AN **1998373329** MEDLINE
DN **98373329** PubMed ID: **9708035**
TI Selectins as new targets for immunoliposome-mediated drug delivery. A potential way of anti-inflammatory therapy.
AU Bendas G; Krause A; Schmidt R; Vogel J; Rothe U
CS Department of Pharmacy, Martin Luther University Halle, Germany.
SO PHARMACEUTICA ACTA HELVETIAE, (1998 Jun) 73 (1) 19-26.
Journal code: 0401134. ISSN: 0031-6865.
CY Switzerland
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199809
ED Entered STN: 19980917
Last Updated on STN: 19980917
Entered Medline: 19980904
AB Endothelial **cell adhesion molecules**, which are expressed in response to inflammatory signals to mediate recruitment of leukocytes to sites of inflammation, appear to be excellent targets for drug delivery systems to open new perspectives of antiinflammatory therapies. In this study we describe the preparation and characterization of antibody-coupled liposomes (immunoliposomes) as directed against endothelial (**E**)-**selectins**. We have examined the factors affecting the covalent coupling of antibodies to the membrane anchor N-glutaryl-phosphatidylethanolamine via amide bound and have compared them to other coupling procedures. The target sensitivity has been demonstrated in a cell-containing in-vitro model, where liposome binding to **selectins** under either static, or simulated blood flow conditions was illustrated by using fluorescence microscopical means. It could be shown that even under shear force conditions liposomes selectively accumulate at **selectin**-containing cells when a specific lipid composition and a certain balance in the lipid/antibody ratio was maintained. Furthermore, the need for polyethylene

glycol-derived lipids to sterically stabilize the liposomes for preventing unspecific liposome attachment to cells has been demonstrated.
CT Check Tags: Animal; Human; Support, Non-U.S. Gov't
*Anti-Inflammatory Agents: AD, administration & dosage
Antibodies
CHO Cells: ME, metabolism
***Drug Delivery Systems**
Hamsters
***Immunoconjugates: ME, metabolism**
Liposomes
Mice
***Selectins: ME, metabolism**
CN 0 (Anti-Inflammatory Agents); 0 (Antibodies); 0 (Immunoconjugates); 0 (Liposomes); **0 (Selectins)**

L103 ANSWER 11 OF 13 MEDLINE
AN **97385183** MEDLINE
DN **97385183** PubMed ID: **9238057**
TI Immunotargeting of liposomes to activated vascular endothelial cells: a strategy for site-selective delivery in the cardiovascular system.
AU Spragg D D; Alford D R; Greferath R; Larsen C E; Lee K D; Gurtner G C; Cybulsky M I; Tosi P F; Nicolau C; Gimbrone M A Jr
CS Vascular Research Division, Department of Pathology, Brigham and Women's Hospital, Boston, MA 02115, USA.
NC PO1-HL48743 (NHLBI)
PO1-HL36028 (NHLBI)
SO PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF THE UNITED STATES OF AMERICA, (1997 Aug 5) 94 (16) 8795-800.
Journal code: 7505876. ISSN: 0027-8424.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199709
ED Entered STN: 19970922
Last Updated on STN: 19970922
Entered Medline: 19970908
AB Endothelial-selective delivery of therapeutic agents, such as drugs or genes, would provide a useful tool for modifying vascular function in various disease states. A potential molecular target for such delivery is **E-selectin**, an endothelial-specific cell surface molecule expressed at sites of activation in vivo and inducible in cultured human umbilical vein endothelial cells (HUVEC) by treatment with cytokines such as recombinant human interleukin 1beta (IL-1beta). Liposomes of various types (classical, sterically stabilized, cationic, pH-sensitive), each conjugated with mAb H18/7, a murine monoclonal antibody that recognizes the extracellular domain of **E-selectin**, bound selectively and specifically to IL-1beta-activated HUVEC at levels up to 275-fold higher than to unactivated HUVEC. **E-selectin**-targeted immunoliposomes appeared in acidic, perinuclear vesicles 2-4 hr after binding to the cell surface, consistent with internalization via the endosome/lysosome pathway. Activated HUVEC incubated with **E-selectin**-targeted immunoliposomes, loaded with the cytotoxic agent doxorubicin, exhibited significantly decreased cell survival, whereas unactivated HUVEC were unaffected by such treatment. These results demonstrate the feasibility of exploiting cell surface activation markers for the endothelial-selective delivery of biologically active agents via immunoliposomes. Application of this targeting approach in vivo may lead to novel therapeutic strategies in the treatment of cardiovascular disease.
CT Check Tags: Human; Support, Non-U.S. Gov't; Support, U.S. Gov't, P.H.S.
Cardiovascular Diseases: DT, drug therapy
Cardiovascular System: DE, drug effects

Cardiovascular System: IM, immunology
Cells, Cultured
Drug Carriers
***Drug Delivery Systems**
E-Selectin: IM, immunology
*Endothelium, Vascular: DE, drug effects
Endothelium, Vascular: IM, immunology
*Interleukin-1: AD, administration & dosage
Liposomes
Recombinant Proteins: AD, administration & dosage
CN 0 (Drug Carriers); **0 (E-Selectin)**; 0 (Interleukin-1); 0 (Liposomes); 0 (Recombinant Proteins)

L103 ANSWER 12 OF 13 MEDLINE
AN 95322068 MEDLINE
DN 95322068 PubMed ID: 7598842
TI Advances in antisense efficacy and delivery.
AU Agrawal S; Akhtar S
CS Pharmaceutical Sciences Institute, Aston University, Birmingham, UK.
SO TRENDS IN BIOTECHNOLOGY, (1995 Jun) 13 (6) 197-9.
Journal code: 8310903. ISSN: 0167-7799.
CY ENGLAND: United Kingdom
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Biotechnology; AIDS
EM 199508
ED Entered STN: 19950822
Last Updated on STN: 19970203
Entered Medline: 19950810
CT Check Tags: Animal; Human
Acquired Immunodeficiency Syndrome: DT, drug therapy
Antiviral Agents: AD, administration & dosage
Antiviral Agents: ME, metabolism
Antiviral Agents: TU, therapeutic use
Biological Transport
Clinical Trials
Cytomegalovirus Infections: DT, drug therapy
Drug Carriers
Drug Design
HIV-1: GE, genetics
Intercellular Adhesion Molecule-1: GE, genetics
Liposomes
*Oligonucleotides, Antisense: AD, administration & dosage
Oligonucleotides, Antisense: ME, metabolism
*Oligonucleotides, Antisense: TU, therapeutic use
Papillomavirus, Human
Papovaviridae Infections: DT, drug therapy
Thionucleotides
Tumor Virus Infections: DT, drug therapy
RN **126547-89-5 (Intercellular Adhesion Molecule-1)**
CN 0 (Antiviral Agents); 0 (Drug Carriers); 0 (Liposomes); 0 (Oligonucleotides, Antisense); 0 (Thionucleotides)

L103 ANSWER 13 OF 13 MEDLINE
AN **95104459** MEDLINE
DN **95104459** PubMed ID: **7805880**
TI Adhesion molecules: a new target for immunoliposome-mediated drug delivery.
AU Bloemen P G; Henricks P A; van Bloois L; van den Tweel M C; Bloem A C; Nijkamp F P; Crommelin D J; Storm G
CS Department of Pharmacology, Utrecht University, The Netherlands.
SO FEBS LETTERS, (1995 Jan 3) 357 (2) 140-4.
Journal code: 0155157. ISSN: 0014-5793.

following irradiation has been shown, but the functional significance of this upregulation in various endothelial cell lines is not clear. We have developed an in vitro flow model to study the functional consequences of the radiation-induced upregulation of E-selectin and intercellular adhesion molecule (ICAM-1). Methods: Human dermal microvascular endothelial cells (HDMEC), human umbilical vein endothelial cells (HUVEC), or transformed human microvascular endothelial cells (HMEC-1) were grown in 35-mm dishes and irradiated with a single dose of 10 Gy. HL-60 (human promyelocytic leukemia) cells were perfused over the irradiated endothelial cells in a parallel plate flow chamber at shear stress ranging from 0.5 to 2.0 dynes/cm2. Flow cytometry was used to quantify the expression of E-selectin and ICAM-1 on the various endothelial cells. Results: Flow cytomeric analysis revealed an upregulation of ICAM-1 expression on all three cell types postirradiation (post-IR), and an upregulation of E-selectin expression only on HDMEC post-IR. E-selectin expression was detected on control HDMEC, but at a lower level than that detected on post-IR HDMEC. Flow assays revealed a significant increase in the number of rolling and firmly adherent HL-60 cells on post-IR HDMEC at shear stress ltoreq1.5 dynes/cm2; pretreatment of control and irradiated HDMEC with antibodies to E-selectin and ICAM-1 significantly diminished the number of rolling and firmly adherent HL-60 cells, respectively. No rolling or firm adhesion of HL-60 cells was observed on HUVEC or HMEC-1 monolayers post-IR. Conclusion: These findings suggest that ICAM-1 is upregulated on irradiated HDMEC, HUVEC, and HMEC-1. E-selectin is upregulated to a functional level only on irradiated HDMEC, and not on irradiated HUVEC or HMEC-1.

CC Cytology and Cytochemistry - General *02502
Cytology and Cytochemistry - Human *02508
Radiation - General *06502
Biochemical Studies - General *10060
Biochemical Studies - Proteins, Peptides and Amino Acids *10064
Cardiovascular System - Physiology and Biochemistry *14504

BC Hominidae 86215

IT Major Concepts
Biochemistry and Molecular Biophysics; Cardiovascular System (Transport and Circulation); Cell Biology; Radiation Biology

IT Chemicals & Biochemicals
E-selectin: expression, functional significance, upregulation; adhesion molecules: expression, functional significance; intercellular adhesion molecule-1: expression, functional significance, upregulation

IT Methods & Equipment
flow cytometry: analytical method, cytophotometry

IT Miscellaneous Descriptors
ionizing radiation

ORGN Super Taxa
Hominidae: Primates, Mammalia, Vertebrata, Chordata, Animalia

ORGN Organism Name
HDMEC cell line (Hominidae): human dermal microvascular endothelial cells; HL-60 cell line (Hominidae); HMEC-1 cell line (Hominidae): human microvascular endothelial cells; HUVEC cell line (Hominidae): human umbilical vein endothelial cells

ORGN Organism Superterms
Animals; Chordates; Humans; Mammals; Primates; Vertebrates

L112 ANSWER 2 OF 7 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
AN **2001:370117** BIOSIS
DN **PREV200100370117**
TI Ligand coated nanosphere adhesion to E- and P-selectin under static and flow conditions.
AU Blackwell, Jonathan E.; Dagia, Nilesh M.; Dickerson, J. Bradley; Berg, Ellen L.; **Goetz, Douglas J. (1)**
CS (1) Department of Chemical Engineering, Ohio University, 172 Stocker Center, Athens, OH, 45701: goetzd@ohio.edu USA

SO Annals of Biomedical Engineering, (2001) Vol. 29, No. 6, pp. 523-533. print.
ISSN: 0090-6964.
DT Article
LA English
SL English
AB The heterogeneous distribution of endothelial cell adhesion molecules (ECAMs) on the lumenal surface of vascular endothelium provides an opportunity to deliver drugs to select tissues. The targeting could be achieved by using carriers whose outer surface has a ligand for a selectively expressed ECAM. The carriers would interact with the edothelium in a fluid dynamic environment and in many of these schemes nanoparticles would be used. It is unclear what role various parameters (e.g., ligand-ECAM chemistry, fluid shear) will have on the adhesion of the nanoparticles to the endothelium. To facilitate studies in this area, we have developed a prototypical in vitro model that allows investigation of nanoparticle adhesion. We coated polystyrene nanospheres with a humanized mAb (HuEP5C7.g2) that recognizes the ECAMs E- and P-selectin. Adhesion assays revealed that HuEP5C7.g2 nanospheres exhibit augmented, specific adhesion to selectin presenting cellular monolayers and that the adhesion can be affected by the fluid shear. These results; (i) strongly suggest that HuEP5C7.g2 could be used to target nanoparticles to selectin presenting endothelium; (ii) demonstrate that fluid shear can affect nanoparticle adhesion; and (iii) define a system which can be used to study the effects of various system parameters on nanoparticle adhesion.
CC Cytology and Cytochemistry - Animal *02506
Cytology and Cytochemistry - Human *02508
Biochemical Studies - Proteins, Peptides and Amino Acids *10064
Biophysics - Bioengineering *10511
Pathology, General and Miscellaneous - Therapy *12512
Cardiovascular System - Physiology and Biochemistry *14504
Pharmacology - General *22002
Pharmacology - Clinical Pharmacology *22005
BC Hominidae 86215
Cricetidae 86310
IT Major Concepts
Biomedical Engineering (Allied Medical Sciences); Pharmacology; Cardiovascular System (Transport and Circulation)
IT Parts, Structures, & Systems of Organisms
vascular endothelium: circulatory system
IT Chemicals & Biochemicals
E-selectin: ligand coated nanosphere adhesion; HuEP5C.g2: humanized monoclonal antibody; P-selectin: ligand coated nanosphere adhesion; drug carriers; endothelial cell adhesion molecules; ligand coated nanosphere
IT Miscellaneous Descriptors
flow conditions; fluid shear; static conditions
ORGN Super Taxa
Cricetidae: Rodentia, Mammalia, Vertebrata, Chordata, Animalia; Hominidae: Primates, Mammalia, Vertebrata, Chordata, Animalia
ORGN Organism Name
CHO cell line (Cricetidae): Chinese hamster ovary cells; CHO-E cell line (Cricetidae): Chinese hamster ovary cells; CHO-P cell line (Cricetidae): Chinese hamster ovary cells; HUVEC cell line (Hominidae): human umbilical vein endothelial cells
ORGN Organism Superterms
Animals; Chordates; Humans; Mammals; Nonhuman Mammals; Nonhuman Vertebrates; Primates; Rodents; Vertebrates

L112 ANSWER 3 OF 7 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
AN **2001:309181** BIOSIS
DN **PREV200100309181**
TI Limited adhesion of biodegradable microspheres to E- and P-selectin under

flow.

AU Dickerson, J. Bradley; Blackwell, Jonathan E.; Ou, Jao J.; Patil, Vivek R. Shinde; **Goetz, Douglas J. (1)**

CS (1) Department of Biomedical Engineering, University of Memphis, Memphis, TN: goetzd@ohio.edu USA

SO Biotechnology and Bioengineering, (June 20, 2001) Vol. 73, No. 6, pp. 500-509. print.
ISSN: 0006-3592.

DT Article

LA English

SL English

AB In a variety of disease settings the expression of the endothelial selectins E- and P-selectin appears to be increased. This feature makes these molecules attractive targets around which to design directed drug-delivery schemes. One possible approach for achieving such delivery is to use polymeric biodegradable microspheres bearing a humanized monoclonal antibody (MAb) for E- and P-selectin, MAb HuEP5C7.g2. Perhaps the simplest technique for "coupling" HuEP5C7.g2 to the microspheres is via nonspecific adsorption. Previous studies suggest, however, that the adsorption of proteins onto microspheres fabricated in the presence of a stabilizer such as poly(vinyl alcohol) (PVA) is limited. It is unclear to what extent this limited level of adsorbed HuEP5C7.g2 would be able to support adhesion to E- and P-selectin under flow conditions. To explore this issue, we prepared microspheres from the biodegradable polymer, poly(epsilon-caprolactone) (PCL), using a single emulsion process and PVA as a stabilizer. We then incubated the PCL microspheres with HuEP5C7.g2 and studied the adhesion of the resulting HuEP5C7.g2 microspheres to E- and P-selectin under in vitro flow conditions. We found that the HuEP5C7.g2 PCL microspheres exhibit specific adhesion to Chinese hamster ovary cells stably expressing P-selectin (CHO-P) and 4-h IL-1beta-activated human umbilical vein endothelial cells (HUVEC). In contrast, HuEP5C7.g2 PCL microspheres exhibit little adhesion to parental CHO cells or unactivated HUVEC. The attachment efficiency to the selectin substrates was quite low, with appreciable attachment occurring only at low shear (0.3 dyn/cm2). Other supporting data strongly suggest that the limited attachment efficiency is due to a low level of HuEP5C7.g2 adsorbed to the PCL microspheres. Although the attachment was limited, a significant percentage of the HuEP5C7.g2 PCL microspheres were able to remain adherent at relatively high shear (8 dyn/cm2). Combined, our data suggest that HuEP5C7.g2 PCL microspheres exhibit selective limited adhesion to cellular substrate expressing E- and P-selectin.

CC Biochemical Studies - General *10060
Cytology and Cytochemistry - General *02502
Cytology and Cytochemistry - Animal *02506
Cytology and Cytochemistry - Human *02508
Biochemical Studies - Proteins, Peptides and Amino Acids *10064
Biochemical Studies - Carbohydrates *10068
Pathology, General and Miscellaneous - Therapy *12512
Pharmacology - General *22002
Pharmacology - Clinical Pharmacology *22005
Immunology and Immunochemistry - General; Methods *34502

BC Hominidae 86215
Cricetidae 86310

IT Major Concepts
Biochemistry and Molecular Biophysics; Cell Biology; Pharmacology

IT Parts, Structures, & Systems of Organisms
cells

IT Chemicals & Biochemicals
E-selectins: molecular binding studies; P-selectins: molecular binding studies; biodegradable microspheres: molecular analysis, preparation, selectin adhesion studies; biodegradable polymers: applications; carbohydrates; ligands; monoclonal antibodies; proteins

IT Miscellaneous Descriptors

biotechnology; drug delivery schemes: applications, design
ORGN Super Taxa
Cricetidae: Rodentia, Mammalia, Vertebrata, Chordata, Animalia; Hominidae: Primates, Mammalia, Vertebrata, Chordata, Animalia
ORGN Organism Name
CHO cell line (Cricetidae); human (Hominidae)
ORGN Organism Superterms
Animals; Chordates; Humans; Mammals; Nonhuman Mammals; Nonhuman Vertebrates; Primates; Rodents; Vertebrates

L112 ANSWER 4 OF 7 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
AN **2001:275482** BIOSIS
DN **PREV200100275482**
TI Extravasation of poly(amidoamine) (PAMAM) dendrimers across microvascular network endothelium.
AU El-Sayed, Mohamed; **Kiani, Mohammad F.**; Naimark, Mike D.; Hikal, Ahmed H.; Ghandehari, Hamidreza (1)
CS (1) Department of Pharmaceutical Sciences, School of Pharmacy, University of Maryland at Baltimore, Baltimore, MD: hghandeh@rx.umaryland.edu USA
SO Pharmaceutical Research (New York), (January, 2001) Vol. 18, No. 1, pp. 23-28. print.
ISSN: 0724-8741.
DT Article
LA English
SL English
AB Purpose: To study the influence of a controlled incremental increase in size and molecular weight of a series of poly(amidoamine) (PAMAM) dendrimers on their extravasation across the microvascular network endothelium. Methods: A series of PAMAM dendrimers (generations 0-4) were fluorescently labeled using fluorescein isothiocyanate (FITC). Purification and fractionation of the fluorescently labeled polymers were done using size exclusion chromatography. The hamster cremaster muscle preparation was used as an in vivo model to study the extravasation process of the fluorescently labeled polymers. The extravasation process was visualized and recorded using intravital microscopy techniques. Analysis of the recorded experiments was done using Metamorph Imaging System. Extravasation of the fluorescently labeled polymers is reported in terms of their extravasation time (tau), i.e., the time needed for the fluorescence intensity in the interstitial tissue to reach 90% of the fluorescence intensity in the neighboring microvessels. Results: Extravasation time (tau) describes the rate of microvascular extravasation of polymeric drug carriers across the microvascular endothelium into the interstitial tissue. Extravasation time (tau) of the studied PAMAM dendrimers showed size and molecular weight dependence. An increase in size and/or molecular weight of PAMAM dendrimers resulted in a corresponding exponential increase in the extravasation time (tau). Conclusions: Extravasation of PAMAM dendrimers across the microvascular endothelium showed size and molecular weight dependence. Results suggest that in addition to size and molecular weight, other physicochemical properties of polymeric drug carriers such as molecular geometry and charge may influence their microvascular extravasation. Systematic studies of the influence of the physico-chemical properties of polymeric drug carriers on their microvascular extravasation will aid in the design of novel macromolecular drug carriers with controlled extravasation profiles.
CC Cardiovascular System - Physiology and Biochemistry *14504
Cytology and Cytochemistry - Animal *02506
Biophysics - Membrane Phenomena *10508
Pathology, General and Miscellaneous - Therapy *12512
Muscle - Physiology and Biochemistry *17504
Pharmacology - General *22002
BC Cricetidae 86310
IT Major Concepts
Membranes (Cell Biology); Pharmacology; Cardiovascular System

(Transport and Circulation)
IT Parts, Structures, & Systems of Organisms
cremaster muscle: muscular system; endothelial barrier: circulatory system; microvascular network endothelium: circulatory system
IT Chemicals & Biochemicals
poly(amidoamine) dendrimers [PAMAM dendrimers]: extravasation, polymeric drug carrier; poly(ethylene glycol): polymeric drug carrier
IT Methods & Equipment
intravital microscopy: microscopy method
IT Miscellaneous Descriptors
drug delivery; microvascular extravasation
ORGN Super Taxa
Cricetidae: Rodentia, Mammalia, Vertebrata, Chordata, Animalia
ORGN Organism Name
hamster (Cricetidae): animal model
ORGN Organism Superterms
Animals; Chordates; Mammals; Nonhuman Mammals; Nonhuman Vertebrates; Rodents; Vertebrates
RN 25322-68-3 (POLY(ETHYLENE GLYCOL))

L112 ANSWER 5 OF 7 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
AN **2001:46265** BIOSIS
DN **PREV200100046265**
TI Late effects of ionizing radiation on the microvascular networks in normal tissue.
AU Nguyen, Vinh; Gaber, M. Waleed; Sontag, Marc R.; **Kiani, Mohammad F. (1)**
CS (1) School of Biomedical Engineering, University of Tennessee, 899 Madison Avenue, Suite 801, Memphis, TN, 38163 USA
SO Radiation Research, (November, 2000) Vol. 154, No. 5, pp. 531-536. print. ISSN: 0033-7587.
DT Article
LA English
SL English
AB Damage to the microvascular networks constitutes one of the most important components of ionizing radiation damage to normal tissue. Previously, we have reported the early (3, 7 and 30 days postirradiation) effects of ionizing radiation on the structure and function of normal tissue microvascular networks. Here we report on the late effects of ionizing radiation on the structural and functional changes in microvascular networks in locally irradiated (single 10-Gy dose) hamster cremaster muscles observed 60, 120 and 180 days postirradiation; age-matched animals were used as controls. As in the previous study, intravital microscopy was used to measure structural and functional parameters in complete microvascular networks in vivo. A factorial design was used to examine the effects of radiation status, time postirradiation, and network vessel type on the structure and function of microvascular networks. Our results indicate that the progression of radiation-induced microvascular damage continues during the late times but that there is partial recovery from radiation damage within 6 months postirradiation. Red blood cell flux, red blood cell velocity, and capillary blood flow in irradiated networks at 180 days postirradiation were significantly greater than control levels. As at the early times, all vessel types were not damaged equally by radiation at every time.
CC Radiation - General *06502
Cytology and Cytochemistry - Animal *02506
Cardiovascular System - Physiology and Biochemistry *14504
Blood, Blood-Forming Organs and Body Fluids - Blood and Lymph Studies *15002
Blood, Blood-Forming Organs and Body Fluids - Blood Cell Studies *15004
Muscle - Physiology and Biochemistry *17504
BC Cricetidae 86310
IT Major Concepts

Muscular System (Movement and Support); Radiation Biology; Cardiovascular System (Transport and Circulation)
IT Parts, Structures, & Systems of Organisms
cremaster muscle: muscular system; microvascular network: circulatory system; red blood cells: blood and lymphatics
IT Miscellaneous Descriptors
ionizing radiation
ORGN Super Taxa
Cricetidae: Rodentia, Mammalia, Vertebrata, Chordata, Animalia
ORGN Organism Name
golden Syrian hamster (Cricetidae): male
ORGN Organism Superterms
Animals; Chordates; Mammals; Nonhuman Mammals; Nonhuman Vertebrates; Rodents; Vertebrates

L112 ANSWER 6 OF 7 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
AN **2000:409486** BIOSIS
DN **PREV200000409486**
TI CD11b/CD18-coated microspheres attach to E-selectin under flow.
AU Crutchfield, Karen L.; Shinde Patil, Vivek R.; Campbell, Craig J.; Parkos, Charles A.; Allport, Jennifer R.; **Goetz, Douglas J. (1)**
CS (1) Department of Chemical Engineering, Ohio University, 181 Stocker Hall, Athens, OH, 45701 USA
SO Journal of Leukocyte Biology, (February, 2000) Vol. 67, No. 2, pp. 196-205. print.
ISSN: 0741-5400.
DT Article
LA English
SL English
AB Neutrophils can attach to E-selectin under flow. Proposed ligands for E-selectin carry SLex-type glycans. The leukocyte beta2 integrins are glycosylated with SLex. Thus, we speculated that beta2 integrins could support attachment to E-selectin. To test this hypothesis, we coated 10-mum-diameter microspheres with purified CD11b/cd18 (alphaMbeta2) and investigated the adhesion of the resulting alphaMbeta2 microspheres to E-selectin. Under in vitro flow conditions, the alphaMbeta2 microspheres attached to Chinese hamster ovary cells expressing E-selectin (CHO-E) and 4-h interleukin-1beta-activated human umbilical vein endothelial cells (HUVEC). At a shear stress of 1.8 dynes/cm2, the attachment events were eliminated by pretreatment of the cellular monolayers with a mAb to E-selectin. alphaMbeta2 microspheres did not attach to untransfected CHO cells or unactivated HUVEC at 1.8 dynes/cm2. Taken together, the results strongly suggest that the CD11b/CD18-E-selectin bond has sufficient biophysical properties to mediate attachment of neutrophil-sized particles to E-selectin under flow.
CC Cytology and Cytochemistry - Animal *02506
Cytology and Cytochemistry - Human *02508
Biochemical Studies - Proteins, Peptides and Amino Acids *10064
Cardiovascular System - Physiology and Biochemistry *14504
Blood, Blood-Forming Organs and Body Fluids - Blood and Lymph Studies *15002
Blood, Blood-Forming Organs and Body Fluids - Blood Cell Studies *15004
Immunology and Immunochemistry - General; Methods *34502
BC Hominidae 86215
Cricetidae 86310
IT Major Concepts
Immune System (Chemical Coordination and Homeostasis)
IT Parts, Structures, & Systems of Organisms
leukocyte: blood and lymphatics, immune system; neutrophil: blood and lymphatics, immune system; umbilical vein endothelial cell: circulatory system
IT Chemicals & Biochemicals
CD11b/CD18; E-selectin; Mac-1; SLe-X-type glycans; beta-2 integrins

IT Methods & Equipment
alpha-M-beta-2 microspheres: equipment
IT Miscellaneous Descriptors
inflammation; neutrophil-size particles: attachment, under flow
ORGN Super Taxa
Cricetidae: Rodentia, Mammalia, Vertebrata, Chordata, Animalia; Hominidae: Primates, Mammalia, Vertebrata, Chordata, Animalia
ORGN Organism Name
CHO cell line (Cricetidae); human (Hominidae)
ORGN Organism Superterms
Animals; Chordates; Humans; Mammals; Nonhuman Mammals; Nonhuman Vertebrates; Primates; Rodents; Vertebrates

L112 ANSWER 7 OF 7 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
AN **1999:437663** BIOSIS
DN **PREV199900437663**
TI Cell-cell adhesive interactions in an in vitro flow chamber.
AU **Goetz, Douglas J. (1)**; Greif, Daniel M.; Shen, Jian; Luscinskas, Francis W.
CS (1) Vascular Research Division, Department of Pathology, Brigham and Women's Hospital, Boston, MA USA
SO Dejana, E. [Editor]; Corada, M. [Editor]. Methods in Molecular Biology, (1999) Vol. 96, pp. 137-145. Methods in Molecular Biology; Adhesion protein protocols.
Publisher: Humana Press Inc. Suite 808, 999 Riverview Drive, Totowa, New Jersey 07512, USA.
ISSN: 0097-0816. ISBN: 0-89603-417-8.
DT Book
LA English
CC Biochemical Methods - General *10050
Methods, Materials and Apparatus, General - Laboratory Apparatus *01006
Biophysics - General Biophysical Studies *10502
Immunology and Immunochemistry - General; Methods *34502
Blood, Blood-Forming Organs and Body Fluids - General; Methods *15001
Cytology and Cytochemistry - Human *02508
BC Hominidae 86215
IT Major Concepts
Cell Biology; Clinical Immunology (Human Medicine, Medical Sciences); Equipment, Apparatus, Devices and Instrumentation; Methods and Techniques
IT Parts, Structures, & Systems of Organisms
leukocyte: adhesion, blood and lymphatics, recruitment, immune system
IT Methods & Equipment
flow chamber assay: Analysis/Characterization Techniques: ct, activity assays, protocol; in vitro flow chamber: laboratory equipment
IT Miscellaneous Descriptors
cell-cell adhesive interactions; inflammation; Book Chapter
ORGN Super Taxa
Hominidae: Primates, Mammalia, Vertebrata, Chordata, Animalia
ORGN Organism Name
human (Hominidae)
ORGN Organism Superterms
Animals; Chordates; Humans; Mammals; Primates; Vertebrates

=> d his

(FILE 'HOME' ENTERED AT 11:15:26 ON 15 AUG 2002)
SET COST OFF

FILE 'HCAPLUS' ENTERED AT 11:15:35 ON 15 AUG 2002
E GOETZ D/AU
L1 39 S E3,E6,E28

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                E KIANI M/AU
L2           13 S E4,E6
L3            4 S L1 AND L2
                E CELL ADHESION MOLECULE/CT
                E E5+ALL
L4         9006 S E6,E7,E5
L5         8336 S E40,E42,E45,E48,E50,E95,E96,E102,E108
                E ICAM/CT
                E E6
                E E3+ALL
L6         4490 S E2
                E ICAM/CT
                E E3+ALL
                E ICAM/CT
                E E7+ALL
                E ICAM/CT
                E E8+ALL
                E ICAM/CT
                E E9+ALL
                E E-SELECTIN/CT
                E E5+ALL
L7         1736 S E2
                E P-SELECTIN/CT
                E E3+ALL
                E P-SELECTIN/CT
                E E7+ALL
L8         1617 S SELECTINS/CT (L) P
                E VCAM/CT
                E E5+ALL
L9         2016 S E2
                E PECAM/CT
                E E5+ALL
L10         610 S E2
                E PECAM/CT
                E E7+ALL
                E ICAM
L11        8892 S E3-E6
L12        8434 S ICAM 1
L13       15025 S CELL? ADHESION MOLECULE
L14        3482 S "E"(S)SELECTIN
L15        3176 S P(S)SELECTIN
                E VCAM
L16        3499 S E3-E5
                E PECAM
L17         920 S E3-E5
L18         398 S INTRACELL? ADHESION MOLECULE
L19         314 S INTRACELL? ADHESION MOLECULE 1
L20        4093 S (VCAM OR PECAM)()1
L21        2188 S VASCUL? CELL? ADHESION MOLECULE
L22        1967 S VASCUL? CELL? ADHESION MOLECULE 1
L23         443 S PLATELET ENDOTHEL? CELL? ADHESION MOLECULE
L24         368 S PLATELET ENDOTHEL? CELL? ADHESION MOLECULE 1
L25        8159 S INTERCELL? ADHESION MOLECULE
L26        7621 S INTERCELL? ADHESION MOLECULE 1
L27       23233 S L4-L26
L28          13 S L1,L2 AND L27
L29           4 S L3 AND L28
                E DRUG DELIVERY/CT
                E E5+ALL
L30      124144 S E3,E2+NT
                E E340+ALL
L31        4698 S E3
                E E12+ALL
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L32          2777 S E5+NT
                  E E8+ALL
L33         12855 S E3
L34         10985 S E8
L35             2 S L28 AND L30-L34
L36             2 S L29 AND TARGET?
L37             2 S L29 AND CARRIER
L38             3 S L35-L37
L39           649 S L27 AND L30-L34
L40           104 S L39 AND CARRIER
L41            45 S L40 AND ENDOTHEL?
L42            66 S L40 AND (ANTIBOD? OR FAB OR MAB)
L43            18 S L40 AND (IR OR ?RADIAT? OR ?RADIO?)
                  E BLOOD VESSEL/CT
                  E E3+ALL
L44         59160 S E5,E4
L45        121107 S E4+NT
L46            34 S L44,L45 AND L40
L47            52 S L41,L46
L48            15 S L47 AND (IR OR ?RADIAT? OR ?RADIO?)
L49             7 S L47 AND 8/SC,SX
L50            19 S L43,L48,L49
                  SEL DN AN 1-3 8 10-13 15-19
L51            13 S E1-E37
L52            15 S L38,L51 AND L1-L51
L53            15 S L52 AND (TARGET? OR BIND? OR CARRIER OR DELIVER? OR DRUG OR P
L54            10 S L52 AND (?NEOPLAS? OR ?TUMOR? OR ?TUMOUR? OR ?CANCER? OR ?CAR
L55             7 S L53,L54 AND  (?CONJUGAT? OR ?COMPLEX?)
L56            15 S L53-L55
L57            10 S L28 NOT L56

     FILE 'HCAPLUS' ENTERED AT 12:47:32 ON 15 AUG 2002

     FILE 'WPIX' ENTERED AT 12:48:08 ON 15 AUG 2002
                  E WO2002030456/PN
L58             1 S E3
L59          6195 S A61K039-00/IC,ICM,ICS
L60          7638 S A61K039-395/IC,ICM,ICS
L61         33722 S (B04-G01 OR C04-G01 OR B04-B04C? OR C04-B04C?)/MC
L62           147 S (B04-H20 OR C04-H20)/MC
L63           911 S L12-L26
                  E ICAM
L64           368 S E3,E4
                  E VCAM
L65           229 S E3,E4
                  E PECAM
L66            31 S E3
L67           375 S L59,L60,L61 AND L62-L66
L68             1 S D05-H10/MC AND L58
L69            31 S A61K047/IC,ICM,ICS,ICA,ICI AND L67
L70            18 S A61K009/IC,ICM,ICS,ICA,ICI AND L67
L71            41 S L58,L68-L70
L72            19 S L71 AND (B14-F02 OR C14-F02 OR B14-H01? OR C14-H01? OR B14-N0
L73            21 S L71 AND (B12-E01 OR C12-E01 OR B14-H? OR C14-H? OR B12-G07 OR
L74            15 S L71 AND P63?/M0,M1,M2,M3,M4,M5,M6
L75            25 S L72-L74
L76            34 S L63 AND L71
L77            22 S L76 AND L75
L78             6 S L71 AND CARRIER
L79             6 S L78 AND L72-L77
L80            35 S L71-L77 NOT L79
L81            29 S L80 AND A61K039/IC,ICM,ICS,ICA,ICI
L82             6 S L80 NOT L81
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L83          41 S L79-L82

     FILE 'WPIX' ENTERED AT 13:11:10 ON 15 AUG 2002

     FILE 'MEDLINE' ENTERED AT 13:12:37 ON 15 AUG 2002
L84       29647 S L63
                E CELL ADHESION MOLECULE/CT
                E E7+ALL
L85       21441 S E22,E47,E52-E56/CT,CN
                E PECAM/CT
                E E4+ALL
L86        1032 S E2/CT,CN
L87       30752 S L84-L86
                E CARRIER/CT
                E E3+ALL
                E DRUG CARRIER/CT
                E E4+ALL
L88       23542 S E20,E25
L89          98 S L87 AND L88
L90           5 S L89 NOT AB/FA
L91           1 S L90 AND DRUG DESIGN/CT
L92          21 S L89 AND C4./CT
L93           4 S L89 AND D22./CT
L94           9 S L89 AND LIGANDS+NT/CT
L95          28 S L89 AND D24.611.125./CT
L96          44 S L92-L95
                E DRUG DELIVERY/CT
                E E5+ALL
L97          98 S E4+NT AND L89
L98          44 S L96 AND L97
                SEL DN AN 1 6 9 12 13 16-18 27
L99           9 S E1-E27
L100         10 S L91,L99 AND L84-L99
L101         54 S L89 NOT L98,L100
                SEL DN AN 15 16 36
L102          3 S E28-E36
L103         13 S L100,L102 AND L84-L102

     FILE 'MEDLINE' ENTERED AT 13:36:35 ON 15 AUG 2002

     FILE 'BIOSIS' ENTERED AT 13:36:44 ON 15 AUG 2002
                E GOETZ D/AU
L104         57 S E3,E6,E21
                E KIANI M/AU
L105         35 S E5,E7
L106         86 S L104,L105
L107         32 S L106 AND CONFERENCE/DT
L108         35 S L106 AND 00520/CC
L109         35 S L107,L108
L110         51 S L106 NOT L109
                SEL DN AN 2-5  7 8 10
L111          7 S E1-E14
L112          7 S L104-L111 AND L111

     FILE 'BIOSIS' ENTERED AT 13:40:24 ON 15 AUG 2002
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